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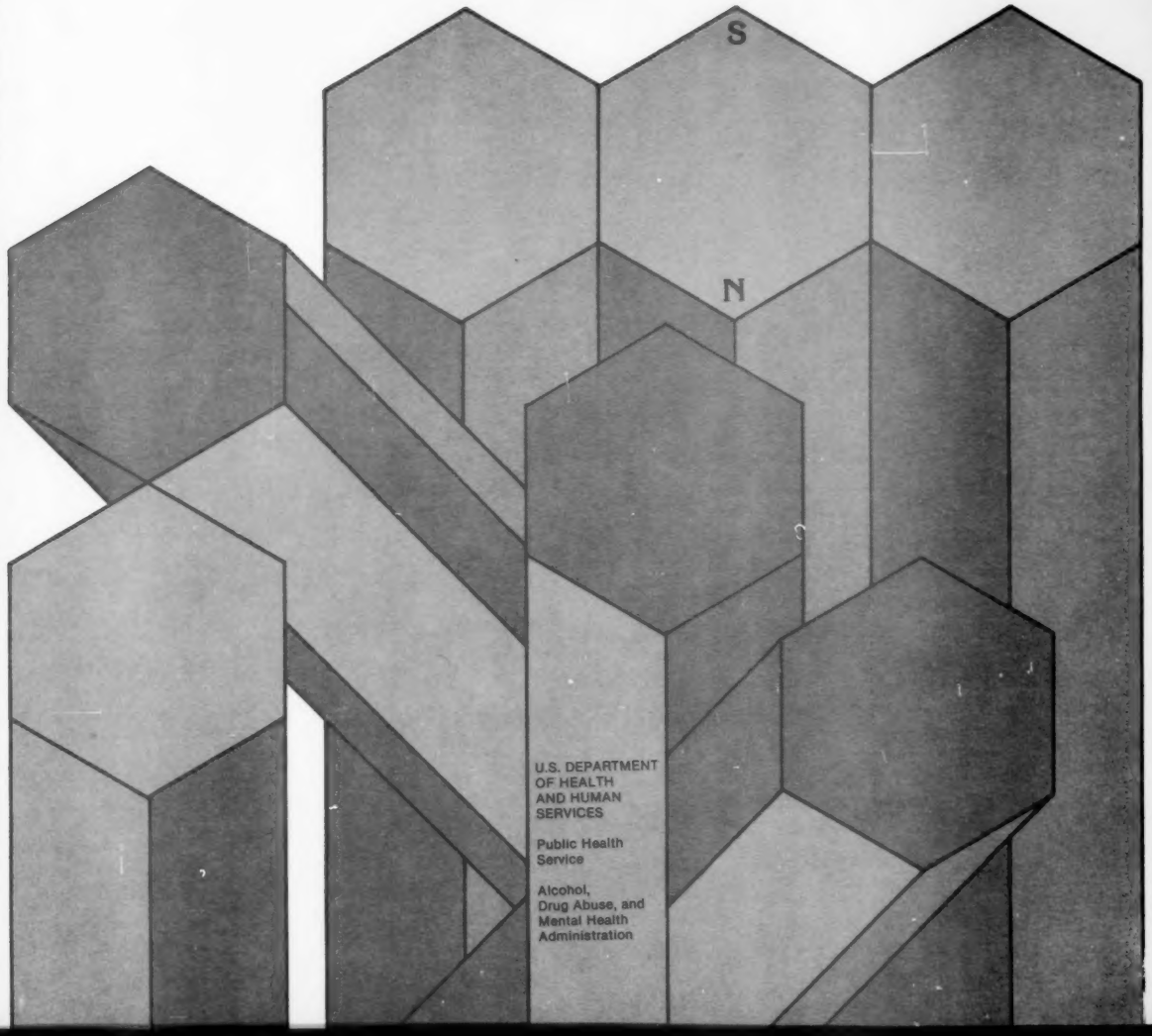
# Psychopharmacology Abstracts



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*Psychopharmacology Abstracts*, is arranged in seventeen categories so that readers may focus more readily on their areas of interest. The Subject and Author Indexes refer the user to the categories under which the abstracts will be found. Thus, in the number 097961 11-14, the first six digits refer to the abstract number, "11" refers to the issue of *Psychopharmacology Abstracts*, and "14" refers to the category.


Carrie Lee Rothgeb, *Editor*
Bette L. Shannon, *Managing Editor*

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# ABSTRACTS

## PRECLINICAL PSYCHOPHARMACOLOGY

### 01 CHEMICAL SYNTHESIS, ISOLATION AND CHARACTERIZATION

**002656** Cheng, S. H.; Shih, J. C. School of Pharmacy, University of Southern California, Los Angeles, CA 90033 **Photoaffinity labeling of serotonin-binding proteins.** Life Sciences 25(26):2197-2203, 1979.

A photosensitive arylazide derivative of serotonin (nitroarylazidophenyl serotonin, NAP-serotonin) was synthesized for use in studying the biochemical nature of serotonin binding sites. (3H)-NAP-serotonin possesses an ability to bind to the crude membranes of rat brains similar to that of 3H-serotonin and therefore seems suitable for use as a photoaffinity labeling probe for serotonin binding sites. Upon irradiation with ultraviolet light, (3H)-NAP-serotonin covalently attaches to protein components of the brain homogenate. Several distinct radioactively labeled proteins were separated by sodium dodecyl sulfate polyacrylamide gel electrophoresis. Their apparent molecular weights were 80,000, 49,000, and 38,000. When 1mcM of unlabeled serotonin or d-lysergic acid diethylamide was added prior to photolysis, the incorporation of (3H)-NAP-serotonin into these proteins was inhibited significantly. No inhibitory effect was observed when dopamine was used. These observations suggest that the photoaffinity labeled proteins are specific for serotonin binding. 10 references. (Author abstract)

**002657** Feeney, Dennis M. Dept. of Psychology, University of New Mexico, Albuquerque, NM 87131 **Marihuana and epilepsy: paradoxical anticonvulsant and convulsant effects.** In: Nahas, G., Marihuana: biological effects. Oxford, Pergamon, 1979. 777 p. (p. 643-657).

The effects of marihuana and cannabinoids on natural and experimental models of epilepsy are reviewed. It is suggested that the psychoactive constituent of cannabis, delta9-tetrahydrocannabinol (THC), paradoxically exerts both a convulsant and anticonvulsant action. For example, it provokes myoclonus, psychomotor, and grand mal seizures in epileptic beagles; however, at comparable doses it blocks maximal electroshock seizures in rats. In contrast, cannabidiol only exerts the anticonvulsant effects and lacks convulsant and psychotropic action. The anticonvulsant action of cannabinoids may result from decreased neural excitability and suppression of posttetanic potentiation. The convulsant action of THC may result from a production of hypersynchronous neural discharge. Given these findings, epileptics should be discouraged from using marihuana due to a risk of provoking seizures. However, because of anticonvulsant potency and lack of convulsant or psychotropic action, cannabidiol should receive clinical trials with epileptic humans as a test of its anticonvulsant effectiveness. 77 references. (Author abstract)

**002658** Huang, Ann; Barker, Jeffery L.; Paul, Steven M.; Moncada, Victoria; Skolnick, Phil. Skolnick: Laboratory of Bioorganic Chemistry, NIAMDD, National Institutes of Health, Bethesda, MD 20205 **Characterization of benzodiazepine receptors in primary cultures of fetal mouse brain and spinal cord neurons.** Brain Research. 190(2):485-491, 1980.

Primary cultures of fetal mouse brain and spinal cord were examined for the presence of binding sites for (3H)diazepam. Both brain and spinal cord cultures contain high affinity binding sites which resemble benzodiazepine receptors found in mammalian CNS with respect to both pharmacologic profile and response to exogenously applied GABA. It is concluded that these observations, coupled with the electrophysiologic properties of these cells suggest that primary cultures of fetal mouse brain and spinal cord may be valid models for studying the role and regulation of the benzodiazepine receptor. 22 references. (Author abstract)

**002659** Schipper, J.; Tilders, F. J. H.; Ploem, J. S. Dept. of Pharmacology, Medical Faculty, Free University, Amsterdam, The Netherlands **A scanning microfluorimetric study on sympathetic nerve fibres: intraneuronal differences in noradrenaline turnover.** Brain Research. 190(2):459-472, 1980.

The quantitative aspects of formaldehyde-induced fluorescence (FIF) of noradrenaline (NA) in sympathetic nerve fibres were studied in whole amount preparations of the iris of the rat. Both static and scanning microfluorimetric measurements showed a close linear relationship between the FIF intensity and the NA content after pharmacological treatment. It is concluded that the turnover of NA is different in various segments of the sympathetic nerve fibres in the rat iris and that the most intensely fluorescent varicosities display the longest chemically determined half-life and the highest turnover rate of NA. 31 references. (Author abstract modified)

**002660** Uebelhack, Ralf; Belkner, Jutta; Seidel, Karl Nervenklinik des Bereichs Medizin (Charite) der Humbolt Universitat zu Berlin, Schumannstrasse 20/21, DDR-104 Berlin, Germany **/Influence of LSD and 5-methoxy-N-N.-dimethyltryptamine on RNA synthesis in the cell nuclei of the rat brain./** Einfluss von LSD und 5-methoxy-N,N-dimethyltryptamin auf die RNS-synthese in Zellkernen aus Ratterhirn. Psychiatrie Neurologie und Medizinische Psychologie. 31(4);194-196, 1979.

The influence of LSD and 5-methoxy-N.N.-dimethyltryptamine (MeODMT) on the RNA synthesis was verified in cell nuclei from rat's brain. LSD and 5-MeODMT inhibited the RNA synthesis within the test period of 30 minutes. This inhibition possibly participates in adaptive neuronal processes occurring in the course of psychoses. 5 references. (Journal abstract)

**002661** Whitlock, James P., Jr.; Augustine, Robert; Schulman, Howard. Dept. of Pharmacology, Stanford University School of Medicine, Stanford, CA 94305 **Calcium-dependent phosphorylation of histone H3 in butyrate-treated HeLa cells. (Unpublished paper).** Research Report, NIMH Grant MH-32752, 1980. 10 p.

A report that Ca2, at physiological concentrations, stimulates the phosphorylation of histone H3 by an endogenous protein kinase in HeLa cell nuclei is presented. In addition, pretreatment of cells with Na butyrate, which increases histone acetylation, selectively increases the susceptibility of histone H3 to phosphorylation by the protein kinase. The results reveal a potential link between histone H3 acetylation and phosphorylation, modifications which are thought to have important effects on chromatin structure and function. The findings also suggest a possible mechanism whereby stimuli at the cell surface (for example, hormones, mitogens, drugs) may influence biochemical events at the level of the nucleus; changes in the intracellular Ca2 concentration may influence the phosphorylation of chromosomal protein, mediated by Ca2 dependent kinases in the nucleus. 24 references.

### 02 DRUG DEVELOPMENT (PRECLINICAL SCREENING)

**002662** Campbell, Michael E.; Ramirez, Linda. Our Lady of the Lake University of San Antonio, San Antonio, TX 78285 **Persistent effects of prenatally administered scopolamine.** Psychological Reports. 46(2):633-634, 1980.

The behavioral effects on offspring of an anticholinergic drug administered chronically during pregnancy were explored. Three groups of pregnant rats were given daily injections of 2.4mg/kg scopolamine, 1.2mg/kg scopolamine, or 1.0 or .5cc saline. A fourth group served as a noninjection control. Treatment was continued throughout pregnancy and 17 offspring were subsequently tested in a shock drinking conflict situation. Results indicate that offspring of the low dose scopolamine group tolerated significantly more shock than other groups. 9 references. (Author abstract modified)

**002663** Cannon, Joseph G.; Perez, Zurilma; Long, John Paul; Rusterholz, David B.; Flynn, Jan R.; Costall, Brenda; Fortune, David H.; Naylor, Robert J. Division of Medicinal Chemistry and Natural Products, College of Pharmacy, University of Iowa, Iowa City, IA 52242 **N-alkyl derivatives of (plus or minus)-alpha-methyldopamine.** Journal of Medicinal Chemistry. 22(8):901-907, 1979.

The biological effects of a series of N-alkylated alpha-methyldopamine derivatives were compared with those of semirigid dopamine cogeners derived from 2-aminotetralin systems. All the alpha-methyldopamine derivatives were inert as central or peripheral dopaminergic agonists in the animal assays used. Some of the compounds did produce powerful and prolonged locomotor hyperactivity following injection into the nucleus accumbens, but this effect was achieved via indirect mechanisms. Conformational analysis is used to explain the lack of direct dopaminergic agonist activity of the alpha-methyldopamine derivatives. 30 references. (Author abstract modified)

**002664** Daisley, Roy W.; Walker, John. School of Pharmacy, Brighton Polytechinic, Brighton, Sussex BN2 4GJ, England **Substituted oxindoles. Pt VII: Oxindole analogues of tryptamine and its derivatives.** European Journal of Medicinal Chemistry. 14(1):47-52, 1979.

A series of oxindole analogues of tryptamine and its derivatives was prepared and tested for pharmacological activity. Several of the compounds produced hyperthermia when given orally to mice at a dose of 100mg/kg. None showed cardiovascular activity, and effects on phenylquinone-induced writhing were inconsistent. Several compounds were active in the hotplate test, and slight appetite suppressant activity was seen with one compound. 19 references.

**002665** Gervais, Christian; Anker, Daniel; Tezenas, Annick; Paheco, Henri; Sollaud, Jean-Yves; Legheand, Jacques. Laboratoire de Chimie biologique, I.N.S.A., bat. 406, 20 avenue Albert Einstein, F-69621 Villeurbanne Cedex, France **/Potential psychotropic drugs. XIII. Novel butyrophenones related to haloperidol./** Psychotropes potentiels. XIII. Nouvelles butyrophenones apparentees a l'haloperidol. European Journal of Medicinal Chemistry. 15(1):71-76, 1980.

Seven new butyrophenones with spiro(2,3-dihydrobenzofuran-3,4'-piperidine) rings and three of their nonspiro derivatives were synthesized and tested for behavioral activity in mice and rats. Some of these haloperidol-like drugs showed neuroleptic activity. Others exhibited only weak cataleptic activity or none at all. 24 references. (Author abstract modified)

**002666** Huber, Joseph W., III; Raymond, Glynn G. Varian, Instrument Division, 5750 Bintliff, Suite 202, Houston, TX 77036 **Additional conclusions on diazepam injectable precipitate: GC-MS confirmation.** Clinical Toxicology. 14(4):439-444, 1979.

The content of the precipitate formed by the dilution of injectable diazepam was investigated by gas chromatography and mass spectrometry. A commercially available diazepam injection was further diluted with sterile water and a precipitate was formed under conditions consistent with clinical practice. The chromatograms showed that the precipitate consisted entirely of diazepam. 11 references.

**002667** Karler, Ralph; Turkanis, Stuart A. Dept. of Pharmacology, University of Utah College of Medicine, Salt Lake City, UT 84132 **Cannabis and epilepsy.** In: Nahas, G., Marihuana: biological effects. Oxford, Pergamon, 1979. 777 p. (p. 619-641).

The treatment of epilepsy with cannabidiol (CBD) was explored in mice, rats, and frogs. In all experiments CBD was compared with phenytoin (PTN) ethosuximide (ETS) and delta9-tetrahydrocannabinol, which despite its psychoactivity, was included because it serves as a reference cannabinoid, and that resulting descriptive information adds to our general knowledge of the drug's CNS effects. The experiments suggest that CBD meets all requirements as a potentially useful drug in the treatment of epilepsy in that the drug is devoid of the psychotoxicity of marihuana and displays a favorable degree of anticonvulsant selectivity over such neurotoxic effects as motor toxicity. Futhermore, it is essentially free of CNS excitatory effects characteristic of most anticonvulsants, including PTN and ETS. 58 references.

**002668** Tachikawa, S.; Harada, M; Maeno, H. Dept. of Pharmacology and Biochemistry, Central Research Laboratories, Yamanouchi Pharmaceutical Co., Ltd. Itabashi-ku, Tokyo 174, Japan **Pharmacological and biochemical studies on a new compound, 2-(7-indenyloxymethyl)morpholine hydrochloride (YM-08054-1), and its derivatives with potential antidepressant properties.** Archives Internationales de Pharmacodynamie et de Therapie. 238(1):81-95, 1979.

The antidepressant properties of a new indene derivative, 2-(7-indenyloxymethyl)morpholine hydrochloride (YM-08054-1) and related compounds were compared with those of tricyclic antidepressants and viloxacine. The potencies of YM-08054-1 in inhibiting uptake of labeled norepinephrine (NE) and 5-hydroxytryptamine (5-HT) into rat brain synaptosomes were similar to those of amitriptyline and imipramine, but other idene derivatives with N-alkylated morpholine rings were less effective. YM-08054-1 was the most potent of the antidepressants examined in inhibiting reserpine-induced facilitation of convulsions and in potentiating 5-hydroxytryptophan-induced syndromes in mice. The inhibitory effect of YM-088054-1 on reserpine-induced hypothermia was weaker than that of amitriptyline or imipramine, suggesting YM-08054-1 has relatively selective effects on 5-HT rather than NE uptake in vivo. The new compound showed no peripheral anticholinergic activity, a weak local anesthetic effect, and low acute toxicity compared to amitriptyline. 32 references. (Author abstract modified)

**002669** Yarbrough, G. G.; Williams, M.; Haubrich, D. R. Merck Institute for Therapeutic Research, West Point, PA 19486 **The neuropharmacology of a novel gamma-aminobutyric acid analog, kojic amine.** Archives Internationales de Pharmacodynamie et de Therapie. 241(2):266-279, 1979.

Kojic amine (KA), a novel GABA analogue, was tested for GABA mimetic activity in several systems. KA selectively displaced 3H-muscimol binding in rat brain membrane preparations, with a relatively high median inhibitory concentration of 4.4mcM. Ka did not alter the binding of 3H-diazepam. Iontophoretically applied KA inhibited the firing of Purkinje cells and of spontaneously active or glutamate activated neurons in cerebral cortex. The inhibitory effects of KA, which were longer lasting than those of GABA, were antagonized by bicuculline and enhanced by 2,4-diamobutyric acid. On the isolated amphibian spinal cord, KA was less than a third as potent as GABA in depolarizing primary afferent terminals; KH also

caused a marked decrease in the dorsal and ventral root potentials evoked by electrical stimulation of an adjacent or corresponding dorsal root. KA was a poor substrate for GABA uptake systems into rat brain synaptosomes, had no effect on GABA release in vitro, and did not inhibit GABA transaminase activity. Results suggest that KA has some GABA mimetic actions, such as hyperpolarization of postsynaptic GABA receptors, but also exerts other pharmacological effects. 22 references. (Author abstract modified)

002670 Zhdanov, Renat I.; Kadenatsi, Igor B.; Moshkovskii, Juri S.; Lavretskaya, Eleonora Ph.; Piruzyan, Leon A. Institute for Biological Testing of Chemical Compounds, Kupavna, Moscow Region 142450, USSR **Pharmacological activity and distribution in vivo of paramagnetic models of some psychotropic compounds.** Life Sciences. 25(26):2163-2171, 1979.

The pharmacological action of paramagnetic models of psychotropic compounds 1-oxyl-2,2,6,6-tetramethyl-4(beta-aminoethyl) piperidine (Ia), 1-oxyl-2,2,6,6-tetramethyl-4-ethylsulphonyl-1,2,5,6-tetrahydropyridine (IIIa) and of their derivatives was studied. The following effects were tested in male mice: 1) acute toxicity of single interperitoneal injection; 2) behavioral effects; 3) effects on orientation motion activity; 4) stimulation of aggressive behavior; 5) effects on the hexenale-induced sleep time; 6) influence on apomorphine, L-DOPA, phenamine, arecoline, nicotine, and haloperidol effects; and 7) effects on corasole and maximal electroshock-induced seizure. Distribution of the paramagnetic models in blood, brain, liver, kidney, and spleen of white rats was also studied by means of the ESR method. Type I compounds caused incorrect behavior, while type III compounds had a pronounced sedative action. All compounds penetrated into all organs at about the same rate, but the concentration of the substances remained higher in the brain for a longer period of time. 11 references. (Author abstract modified)

## 03 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

002671 Advokat, Claire. Dept. of Pharmacology, University of Illinois College of Medicine, P.O. Box 6998, Chicago, IL 60680 **Evidence for conditioned tolerance of the tail flick reflex.** Behavioral and Neural Biology. 29(3):385-389, 1980.

The conditioning model of tolerance of the tail reflex was examined in Sprague-Dawley rats. Behavioral tolerance of the tail flick reflex to the analgesic action of morphine was significantly modified by the context in which the reflex was assessed. Animals tested in a familiar environment, in which they had regularly received the drug, were significantly more tolerant than animals tested in a novel environment in which the drug had never been given. 10 references. (Author abstract)

002672 Aghajanian, G. K. Connecticut Mental Health Center, 34 Park Street, New Haven, CT 06508 **Mescaline and LSD facilitate the activation of locus coeruleus neurons by peripheral stimuli.** Brain Research. 186(2):492-498, 1980.

The effects of mescaline and D-lysergic acid diethylamide (LSD) on the firing of noradrenergic neurons of the locus coeruleus (LC) were examined in male albino rats. Both drugs depressed the spontaneous activity of LC neurons, but increased their reactivity to the excitatory influences of peripheral stimuli. Desipramine, clonidine, and L-amphetamine, which also reduce spontaneous LC firing, did not enhance responsivity to stimuli. Methysergide, a nonpsychedelic analogue of LSD, was also ineffective. Preliminary microiontophoretic studies suggest that the effects of LSD and mescalne are mediated through an effect on LC afferents rather than by an increase in the excitability of LC neurons themselves. 38 references.

002673 Aguilar, Jose S.; Criado, Manuel; De Robertis, E. Instituto de Biologia Celular, Facultad de Medicina, Universidad de Buenos Aires, 1121 Buenos Aires, Argentina **Action of detergents on 3H-dihydroergokriptine binding and localization of alpha-adrenoceptors in synaptosomal membranes.** European Journal of Pharmacology. 61(1):47-53, 1980.

The effects of detergents on the binding of tritiated dihydroergokriptine (3H-DHE) to alpha-adrenoceptors in the cat basal ganglia were examined. Low concentrations of deoxycholate, digitonin, or Nonidet P-40 stimulated 3H-DHE binding to synaptosomal membranes, but higher concentrations of the detergents inhibited binding. The 3H-DHE specific radioactivity was reduced by Triton X-100 at concentrations (0.1 to 0.2%) that affected only the presynaptic membrane and was further reduced by a concentration (0.5%) that disintegrated the postsynaptic membrane. Results suggest that alpha-adrenergic receptors may be localized at both the presynaptic and postsynaptic membranes of central synapses. 18 references. (Author abstract modified)

002674 Aguilar, Jose S.; Criado, Manuel; De Robertis, E. Instituto de Biologia Celular, Facultad de Medicina, Universidad de Buenos Aires, Buenos Aires, Argentina **Protection by atropine of the inhibition caused by Trition X-100 on central muscarinic receptors.** European Journal of Pharmacology. 63(4):251-257, 1980.

Tritiated quinuclidinyl benzylate (3H-QNB) labeled a single type of binding site in synaptosomal membranes from cat cerebral cortex. Triton X-100 inhibited the specific binding of 3H-QNB, but atopine protected the receptor site from the inhibitory action of the detergent. Results indicate that muscarinic cholinergic receptors are located both presynaptically and postsynaptically. 12 references. (Author abstract modified)

002675 Akaishi, Takao; Negoro, Hideo; Kobayasi, Syoiti. Dept. of Physiology, Niigata University School of Medicine, Niigata 951, Japan **Responses of paraventricular and supraoptic units to angiotensin II, Sarl-Ile8-angiotensin II and hypertonic NaCl administered into the cerebral ventricle.** Brain Research. 188(2):499-511, 1980.

The responses of neurosecretory units in the paraventricular and supraoptic nuceli of female Wistar rats to intracerebroventricular administration of angiotensin-II (AII), Sar1-I1e8-angiotensin-II, or hypertonic sodium chloride were examined. Results indicate that AII activates neurosecretory cells by stimulating specific AII receptors in the brain and that AII has a synergistic action with hypertonic sodium chloride. The competitive AII antagonist Sar1-I1e8-angiotensin-II inhibited the spontaneous activity of neurosecretory cells, suggesting endogenous AII may participate in maintenance of basal activity of these cells. 41 references. (Author abstract modified)

002676 Akil, Huda; Hewlett, William A.; Barchas, Jack D.; Li, Choh Hao. Mental Health Research Institute, University of Michigan, Ann Arbor, MI 48109 **Binding of 3H-beta-endorphin to rat brain membranes: characterization of opiate properties and interaction with ACTH.** European Journal of Pharmacology. 64(1);1-8, 1980.

The binding of tritiated beta-endorphin to rat brain homogenates was saturable, stereospecific, of high affinity, and inhibited by sodium. The dissociation rate for beta-endorphin was 10 times longer than that of naloxone. The regional distribution of beta-endorphin binding differed from that of naloxone and enkephalin. ACTH1-24 was more effective in displacing beta-endorphin than naloxone. 17 references. (Author abstract modified)

**002677** Albert, D. J.; Madryga, F. J. Psychology Dept., University of British Columbia, Vancouver, British Columbia V6T 1W5, Canada **An examination of the functionally effective spread of 4 mcl of slowly infused lidocaine.** Behavioral and Neural Biology. 29(3):378-384, 1980.

Infusions of 4mcl of the local anesthetic lidocaine (2%) over a 15 min period were made in or adjacent to the oculomotor nucleus of the brain stem in an attempt to establish the functionally effective spread of the lidocaine. Infusions consistently produced complete ipsilateral dialation only when made within 0.5mm of the ipsilateral nucleus. Complete contralateral dilation occurred only when the infusions were made within 0.25mm of the center of the contralateral nucleus. These results agree with previous behavioral indications that slow infusion of relatively large volumes of the local anesthetic lidocaine do not produce a functional block over as large an area as would be predicted from volume considerations alone. 15 references. (Author abstract)

**002678** Altiere, Ralph J.; Inchiosa, Mario A., Jr. Inchiosa: Dept. of Pharmacology, New York Medical College, Valhalla, NY 10595 **Concentration-dependent inhibition of myosin ATPase by an indole metabolite of epinephrine.** Life Sciences. 26(18):1523-1534, 1980.

An indole metabolite of epinephrine (an isomer of adrenochrome) was shown to be a potent inhibitor of myosin, actomyosin, and myofibrillar ATPase when assayed at or near physiologic ionic strength and pH. The inhibition of actomyosin ATPase by this epinephrine derivative was demonstrated to be competitive in nature. Complete inhibition of ATPase activity was never achieved under physiological conditions; maximum inhibition was 50% to 60%. It is concluded that the inhibitor reduced ATPase activity by reversibly attaching to sulfhydryl groups associated with ATPase activity. The reduction of ATPase activity by 50% may be explained by the known heterogeneity of the ATPase sites on myosin; only one half of these sites may be sensitive or accessible to the inhibitor in the state of aggregation of myosin at physiological ionic strength. The inhibitor was found to have no effect on hog cerebral cortex Na, K activated ATPase. These results further support the hypothesis that this inhibitory indole metabolite of epinephrine (which is formed only in smooth muscles relaxed by epinephrine) may be part of the mechanism by which epinephrine produces relaxation in certain smooth muscles. 41 references. (Author abstract modified)

**002679** Arbilla, S.; Langer, S. Z. Langer: Biology Dept. Synthelabo (L.E.R.S.), 58, rue de la Glaciere F-75013 Paris, France **Influence of monoamine oxidase inhibition on the release of 3H-dopamine elicited by potassium and by amphetamine from the rat substantia nigra and corpus striatum.** Naunyn-Schmiedeberg's Archives of Pharmacology. 311(1):45-52, 1980.

The effects of monoamine oxidase (MAO) inhibition on the release of tritiated dopamine (DA) evoked by amphetamine or potassium from the male rat substantia nigra and corpus striatum were examined. Potassium and amphetamine were both more effective in evoking 3H-DA release from the striatum than from the substantia nigra. The MAO inhibitor pargyline increased tissue labeling with 3H-DA in both regions and facilitated the induced release of 3H-DA. Pargyline enhanced potassium evoked release of 3H-DA at the level of DA nerve terminals, but had no effect on potassium evoked release from cell bodies and dendrites. 30 references. (Author abstract modified)

**002680** Arnt, Jorn; Scheel-Kruger, Jorgen. H. Lundbeck & Co. A/S, Ottiliavej 7, DK-2500 Copenhagen, Denmark **Intranigral GABA antagonists produce dopamine-independent biting in rats.** European Journal of Pharmacology. 62(1):51-61, 1980.

Biting, teeth chattering, and chewing were observed in male Wistar rats following bilateral intranigral administration of the GABA antagonists bicuculline methiodide (BMI), picrotoxin, and isopropylbicyclosphosphate. Subthreshold doses for biting induced locomotor activity and sniffing. Biting induced by intranigral BMI was antagonized by concomitant intranigral injection of GABA agonists, but not by catecholamine depletion or dopamine receptor blockade. BMI-induced biting was also antagonized by systemic administration of diazepam or gamma-acetylenic GABA. 49 references. (Author abstract modified)

**002681** Arrigo-Reina, Rose; Ferri, Sergio. University of Catania, Catania, Italy **Evidence of an involvement of the opioid peptidergic system in the reaction to stressful conditions.** European Journal of Pharmacology. 64(1):85-88, 1980.

Cold restraint stress reduced the paw oedema induced in male Sprague-Dawley rats by a local injection of carrageenin, and this effect was reversed by pretreatment with naloxone (5mg/kg). Naloxone also increased the intensity of gastric damage in rats exposed to cold restraint, whereas morphine (10mg/kg) markedly reduced gastric damage in stressed rats. Results suggest that the opioid peptidergic system is involved in the body's reactivity to stressful stimuli. 11 references. (Author abstract modified)

**002682** Ary, Thomas E.; Komiskey, Harold L. Komiskey: Washington State University, College of Pharmacy, Pullman, WA 99164 **Basis of phencyclidine's ability to decrease the synaptosomal accumulation of 3H-catecholamines.** European Journal of Pharmacology. 61(4):401-405, 1980.

The effects of phencyclidine (PCP) on the accumulation of 3H-norepinephrine (3H-NE) in mixed cortical and hypothalamic synaptosomes and on the accumulation of 3H-dopamine (3H-DA) in striatal synaptosomes of male Sprague-Dawley rats were examined. Results show that PCP decreased the accumulation of 3H-NE into mixed cortical/hypothalamic synaptosomes by blocking the uptake of the tritiated amine. In contrast, part of the PCP-induced decrease in accumulation of 3H-DA in striatal synaptosomes appeared to be due to the release of previously accumulated 3H-DA. 11 references. (Author abstract modified)

**002683** Assumpcao, J. A.; Bernardi, N.; Brown, J.; Stone, T. W. Dept. of Physiology, Escola Paulistade Medicina Sao Paola, R. Botucatu, 862, Sao Paolo, Brazil **Selective antagonism by benzodiazepines of neuronal responses to excitatory amino acids in the cerebral cortex.** British Journal of Pharmacology. 67(4):563-568, 1979.

The effects of chlordiazepoxide (CDPX) and diazepam on neuronal responses to acetylcholine (ACh) and to excitatory and inhibitory amino acids were examined in male Porton Wistar rats anesthetized with urethane. CDPX applied by microiontophoresis reduced responses of cortical neurons to glutamate and aspartate, but did not alter responses to ACh. GABA and taurine responses were reduced in only 4 of 25 units tested. Intravenously injected diazepam reduced responses to GABA and taurine in 3 cells but did not alter responses in 11 cells. Of Purkinje cells in the cerebellum, 5 of 16 units showed a substantial increased in responses to GABA and taurine following intravenous or inotophoretic application of the benzodiazepines. It is suggested that the highly selective reduction of excitatory amino acids responses in the cerebral cortex may be related to the behavioral effects of the benzodiazepines. 26 references. (Author abstract modified)

**002684** Astrup, Jens; Blennow, Gosta; Nilsson, Bengt. Laboratory of Experimental Brain Research, University of Lund, Lund, Sweden **Effects of reduced cerebral blood flow upon EEG pattern, cerebral extracellular potassium, and energy metabolism in the rat cortex during bicuculline-induced seizures.** Brain Research. 177(1):115-126, 1979.

Cerebral functional and metabolic changes were determined in male Wistar rats when cerebral blood flow was progressively reduced during status epilepticus induced by bicuculline. Moderate reductions of blood pressure (BP) were accompanied by tissue lactate accummulation and a decrease in the rate of reuptake of potassium ions (K) extruded during discharges. These changes were pronounced at BP about 50mm Hg when the energy state also showed some deterioration and EEG activity changed from bursts and suppressions to single spikes. EEG activity was abolished at BP near 30mm HG, and at a slightly lower BP level a severe energy depletion and massive K release were observed. Results show an increased susceptibility to ischemia during seizures, with changes of membrane pump function and energy metabolism appearing at moderate reductions of BP. 34 references. (Author abstract modified)

**002685** Audigier, Y.; Mazarguil, H.; Gout, R.; Cros, J. Laboratoire de Pharmacologie et de Toxicologie Fondamentales, CNRS, 205 route de narbonne, F-31 078 Toulouse Cedex, France **Structure-activity relationships of enkephalin analogs at opiate and enkephalin receptors: correlation with analgesia.** European Journal of Pharmacology. 63(1):35-46, 1980.

The relationship between the chemical structure, catabolism, relative affinity, biological activity in isolated organs, and analgesic activity after intracerebroventricular injection into male Sprague-Dawley rats was examined for a series of enkephalin analogues. With compounds containing the same C-terminal amino acid as enkephalins (methionine or leucine), there was a good correlation between activity on mu-receptors and antinociceptive activity. However, when proline was the C-terminal amino acid, antinociceptive activity was enhanced with no increase in affinity. 33 references. (Author abstract modified)

**002686** Avakian, Edward V.; Horvath, Steven M. Institute of Environmental Stress, University of California, Santa Barbara, CA 93106 **Plasma catecholamine responses to tyrosine hydroxylase inhibition and cold exposure.** Life Sciences. 26(20):1691-1696, 1980.

The acute effect of alpha-methyl-p-tyrosine (alphaMPT), a tyrosine hydroxylase inhibitor, on plasma levels of norepinephrine (NE), epinephrine (E), dopamine (DA), and adrenal cholesterol content in male rats at room temperature (24 degrees C) and during acute cold exposure (4 degree C) was evaluated. Compared to saline treated controls, alphaMPT: 1) significantly reduced plasma NE and DA in both normal and cold stress conditions, 2) significantly increased plasma E in both environments, and 3) stimulated the adrenal cortex. These findings suggest that tyrosine hydroxylase inhibition and consequent catecholamine synthesis blockade disrupts the homeokinesis of adrenergic processes and may present a significant stress to the intact animal. 14 references. (Author abstract)

**002687** Aveldano-de-Caldironi, Marta I.; Bazan, Nicolas G. Instituto de Investigacions Bioquimicas, Universidad Nacional del Sur 8000-Bahia Blanca, Argentina **Alpha-methyl-p-tyrosine inhibits the production of free arachidonic acid and diacylglycerols in brain after a single electroconvulsive shock.** Neurochemical Research. 4(2):213-221, 1979.

A single electroconvulsive shock (ECS) significantly enlarged the free fatty acid (FFA) pool of the BALB/c mouse brain, with arachidonic acid the most actively released FFA. Pretreatment with alpha-methyl-p-tyrosine (aMT) decreased the endogenous levels of FFA 25 seconds after decapitation and abolished the effect of ECS: the aMT effect was most pronounced for arachidonic acid. A similar but less pronounced effect was observed for mouse brain diacylglycerols (DG). In contrast to ECS, the aMT treatment did not affect the marked release of FFA aand DG in the 3 minutes after decapitation. Results are discussed in relation to the involvement of FFA and DG in neurotransmission and the relationship between biogenic amines and membrane lipid breakdown during electrical stimulation. 26 references. (Author abstract modified)

**002688** Babb, Thomas L.; Perryman, Kent M.; Lieb, Jeffrey P.; Finch, David M.; Crandall, Paul H. Brain Research Institute, University of California Center for Health Sciences, Los Angeles, CA 90024 **Procaine-induced seizures in epileptic monkeys with bilateral hippocampal foci.** Electroencephalography and Clinical Neurophysiology. 47(6):725-737, 1979.

Procaine-induced seizures in epileptic monkeys with bilateral hippocampal foci were examined. Intravenous procaine HCl given at doses of 10mg/kg evoked unilateral or bilateral limbic activation and generalized seizures. At higher doses, bilateral limbic activation of brief seizures occurred. The unilateral onset psychomotor seizures were not identical to spontaneous psychomotor seizures, and the generalized seizures never occurred spontaneously in these monkeys. It is concluded that procaine challenges may selectively activate limbic epileptogenic areas without activation of debilitating generalized tonic/clonic seizures. 18 references. (Author abstract modified)

**002689** Bagchi, Sakti P.; Bagchi, Preeti; Smith, Thomas M. Rockland Research Institute, Orangeburg, NY 10962 **Release of synaptosomal dopamine formed from tyrosine and L-DOPA.** Brain Research. 187(2):403-414, 1980.

The release of (3H)dopamine formed from (3H)DOPA and of (14C)dopamine formed from (14C)tyrosine from synaptosomal preparations from female Wistar rat caudate nuclei were compared. Reserpine, dopamine, serotonin, and 5-hydroxytryptophan had similar effects on (3H)dopamine and (14C)dopamine release, but amfonelic acid and amphetamine acted preferentially on (3H)dopamine. Results suggest that dopamine synaptosomally formed from L-DOPA may exist in a pool distinct from dopamine arising from tyrosine hdyroxylation, and that this dopamine compartmentalization does not involve serotoninergic particles. 22 references. (Author abstract modified)

**002690** Bakhit, Charles; Kwok, Yan C.; Gibb, James W. Dept. of Biochemical Pharmacology and Toxicology, University of Utah, Salt Lake City, UT 84112 **Effects of methamphetamine on kinetic characteristics of neostriatal tyrosine hydroxylase.** Life Sciences. 26(21):1815-1819, 1980.

The effects of methamphetamine on kinetic characteristics of neostriatal tyrosine hydroxylase were investigated in rats. The Vmax of the enzyme was markedly decreased after large, repeated doses of methamphetamine, but no change in the Km for pteridine cofactors nor for the substrate, tyrosine, was detected. It is noted that the decrease in Vmax with methamphetamine was independent of the phosphorylated state of the enzyme. Various hypotheses concerning the mechanisms by which methamphetamine decreases tyrosine hydroxylase activity are discussed. 14 references. (Author abstract modified)

**002691** Balsara, J. J.; Jadhav, J. H.; Chandorkar, A. G. Dept. of Pharmacology, V. M. Medical College, Solapur, Maharashtra 413003, India **Effect of drugs influencing central serotonergic mechanisms on haloperidol-induced catalepsy.** Psychopharmacology. 62(1):67-69, 1979.

Evidence is presented that pretreatment with quipazine, a serotonin agonist, and clomipramine, a selective serotonin neuronal uptake blocker, potentiate the cataleptic effect of haloperidol in a dose dependent manner in rats. Pretreatment with methylsergide, a serotonin antagonist, reduces the cataleptic effect of haloperidol. The results indicate that the cataleptic effect of neuroleptics depends on the balance between the dopaminergic and serotonergic systems, and that the serotonergic system exerts an inhibitory influence on the dopaminergic system. 17 references. (Author abstract)

**002692** Bando, T.; Zambelli, A.; Spencer, W. A. Dept. of Biophysical Engineering, Faculty of Engineering Science, Osaka University, Toyonaka, Osaka, Japan **Rebound excitation and the rhythmic activity of the ventrobasal complex of the thalamus.** Brain Research. 192(1):29-38, 1980.

Membrane potential changes of 18 thalamocortical relay (TCR) cells of the ventrobasal complex of the cat thalamus were recorded intracellularly during rhythmic thalamic activities under moderate barbiturate anesthesia. A single cutaneous stimulus evoked an initial excitatory postsynaptic potential (EPSP) followed by a long-lasting inhibitory postsynaptic potential (IPSP). On the late declining phase of the IPSP, clustered rapidly rising depolarizations (RDs) were seen to generate a burst of spike potentials. The cluster of depolarizations was often followed by an IPSP, and another cycle of IPSPs and RDs were also evoked by a single cortical stimulus. Spontaeous occurrence of RDs was observed. The temporal correlation between the occurrence of RDs and that of the spike potentials was noted. Chloride ions were injected into the TCR cell through the recording microelectrode to eliminate the membrane hyperpolarization which would initiate the postanodal exaltation. After inversion of the IPSPs, RDs remained in the similar phase of rebound excitation to that before the reversal of the IPSPs. It is concluded that excitatory inputs to TCR cells play an important role for the generation of the rhythmic discharges of TCR cells. 22 references. (Author abstract modified)

**002693** Banks, B. E. C.; Brown, C.; Burgess, G. M.; Burnstock, G.; Claret, M.; Cocks, T. M.; Jenkinson, D. H. Dept. of Physiology, University College, London, England **Apamin blocks certain neurotransmitter-induced increases in potassium permeability.** Nature. 282(5737):415-417, 1979.

The effects and mechanism of action of apamin, a neurotoxic polypeptide of known structure derived from bee venom, in abolishing the hyperpolarizing action of externally applied adenosine 5'triphosphate (ATP) on visceral smooth muscle and the hypolarization that follows stimulation of the nonadrenergic inhibitory nerve supply to these tissues, were explored. Results confirm that nanomolar concentrations of apamin reduced inhibition by ATP and by nonadrenergic nerve stimulations, but further experiments suggest that, rather than acting as a specific blocker of ATP receptors, apamin inhibits the increase in potassium permeability caused by a number of agents, including ATP. 24 references. (Author abstract modified)

**002694** Banning, Jon W.; Uretsky, Norman J.; Patil, Popat N.; Beal, Jack L. College of Pharmacy, Ohio State University, Columbus, OH 43210 **Reticuline: a dopamine receptor blocker.** Life Sciences. 26(24):2083-2091, 1980.

It is reported that reticuline, a benzylisoquinoline alkaloid, inhibited specific (3H)-dopamine binding to dopamine receptors in tissue homogenates from rat corpora striata. The alkaloid blocked amphetamine-induced circling behavior in mice with unilateral degeneration of dopaminergic neurons in the corpus striatum. Blockade of apomorphine-induced climbing behavior by reticuline was observed in mice. Reticuline did not produce catalepsy at doses which blocked circling behavior. Results indicate that reticuline is a dopamine receptor blocking agent in the central nervous system. 16 references. (Author abstract modified)

**002695** Baranyi, A.; Feher, O. Dept. of Comparative Physiology, P.O. Box 533, Szeged 6701, Hungary **Convulsive effects of 3-aminopyridine on cortical neurons.** Electroencephalographyand Clinical Neurophysiology. 47(6):745-751, 1979.

The effects of 3-aminopyridine (3-AP) on pyramidal tract neurones in the motor cortex of anesthetized cats were examined. 3-AP proved to be a strong convulsive agent. Local application of 3-AP resulted in typical paroxysmal alterations of neuronal activity. The components of 3-AP action may account for the whole symptomatology of cortical seizures. It is suggested that the use of 3-AP for creation of models of cortical convulsions seems promising. 45 references. (Author abstract modified)

**002696** Barlow, R. B.; Birdsall, N. J. M.; Hulme, E. C. Dept. of Pharmacology, University of Bristol, Bristol, England **Temperature coefficients of affinity constants for the binding of antagonists to muscarinic receptors in the rat cerebral cortex.** British Journal of Pharmacology. 66(4):587-590, 1979.

The temperature coefficients of binding of a series of muscarinic antagonists to their receptors in membrane preparations from the rat cerebral cortex was examined. At 37 degrees C, the affinity constants agreed with those determined by antagonism of acetylcholine-induced contractions of the guinea-pig ileum. The temperature dependence of the affinity constant was low: affinity constants at 0 degrees C differed by less than a factor of three from those measured at 37 degrees C. Results indicate that estimates of the temperature coefficient of binding of antagonists to receptors in ileum strips and in cerebral cortex are qualitatively similar. 7 references. (Author abstract modified)

**002697** Barton, Christopher; Basbaum, Allan I.; Fields, Howard L. Fields: Dept. of Neurology, M-794, School of Medicine, University of California, San Francisco, CA 94143 **Dissociation of supraspinal and spinal actions of morphine: a qualitative evaluation.** Brain Research. 188(2):487-498, 1980.

Opiate suppression of spinal withdrawal reflexes was tested in rats with lesions of the dorsolateral funiculus (DLF), dorsal columns, or ventral quadrant (VQ) or with sham lesions. None of the lesions altered baseline latency of tail flick to noxious heat. Analgesia induced by morphine (5 to 15mg/kg i.p.) was consistently antagonized only by the DLF lesions, but VQ lesions were somewhat effective. Results indicate that spinal and supraspinal sites both contribute significantly to the analgesia induced by systemic administration of morphine. 46 references. (Author abstract modified)

**002698** Battistin, Leontino; Varotto, Mary; Tezzon, Frediano; Pistollato, Luisa. Dept. of Neurology and Psychiatry, University of Padova Medical School, Padua, Italy **Levels and uptake of taurine in various brain regions after drug-induced generalized convulsions.** Neurochemical Research. 4(4):457-464, 1979.

In a study of the role of taurine in the genesis of epilepsy, the effects of metrazol-induced convulsions on the uptake and distribution of taurine in mouse and rabbit brain were measured. In vivo, no significant uptake of taurine was found in mouse brain; while in rabbit brain significant uptake of taurine was found in most areas. The physiological levels of taurine were much higher in mouse than in rabbit brain. In vivo, regional levels and the uptake of taurine were not significantly changed after generalized convulsions. Uptake in vivo was lowered in slices obtained from metrazol treated mice. The lack of effect of metra-

zol convulsions on cerebral taurine in vivo indicated that further study is needed to clarify the relationship between taurine, a putative inhibitory transmitter, and epilepsy. 27 references. (Author abstract)

**002699** Baudry, M.; Martres, M. P.; Schwartz, J. C. Schwartz: Unite 109 de Neurobiologie, Centre Paul Broca de l'INSERM, 2ter, rue d'Alesia, F-75014 Paris, France **3H-Domperidone: a selective ligand for dopamine receptors.** Naunyn-Schmiedeberg's Archives of Pharmacology 308(3):231-237, 1979.

Tritiated domperidone bound with high affinity to an apparently homogenous population of noninteracting sites in a particulate fraction of mouse striatum was studied. Association was rapid and dissociation was relatively slow (half-life, 4 minutes). Analyses of binding kinetics and saturation of binding sites revealed a dissociation constant value of 0.7nM. The relative potencies of various dopamine receptor agonists or antagonists in inhibiting 3H-domperidone binding paralleled their pharmacological activity. Nondopaminergic agents failed to inhibit 3H-domperidone binding. Saturable 3H-domperidone binding was almost entirely inhibited by apomorphine in various nonstriatal regions of mouse brain. Results suggest that 3H-domperidone is a selective ligand for cerebral dopamine receptors. 24 references. (Author abstract modified)

**002700** Bhargava, Hemendra N. Dept. of Pharmacognosy and Pharmacology, University of Illinois at the Medical Center, Chicago, IL 60612 **Cyclo (Leucylglycine) inhibits the development of morphine induced analgesic tolerance and dopamine receptor supersensitivity in rats.** Life Sciences. 27(2):117-123, 1980.

Intraperitoneal administration of cyclo (leucylglycine) prior to and during chronic morphinization in male Sprague-Dawley rats was found to inhibit the development of tolerance to the analgesic effect of morphine and to inhibit the development of dopamine receptor supersensitivity. Rats were rendered tolerant to morphine by subcutaneous implantation of four morphine pellets, each containing 75mg of morphine free base, over a 3 day period. The development of tolerance was evidenced by decreased response to morphine and inhibition of tolerance by the greater analgesic response. Cyclo (leucylglycine) also antagonized the decrease in motor activity (sedation) during morphine withdrawal. Dopamine receptor sensitivity was enhanced in morphine tolerant rats as measured by apomorphine-induced increases in spontaneous motor activity. Cyclo (leucylglycine) administration also blocked dopamine receptor supersensitivity induced by chronic morphinization. It is concluded that development of tolerance to opiates may be associated with enhanced dopamine receptor sensitivity, since both the phenomena were blocked by cyclo (leucylglycine). 21 references. (Author abstract modified)

**002701** Biegon, Anat; Samuel, David. Dept. of Isotope Research, Weizmann Institute of Science, Rehovot, Israel **Binding of a labeled antidepressant to rat brain tissue.** Biochemical Pharmacology. 28(23):3361-3366, 1979.

The binding of a labeled antidepressant, (3H)desipramine, to rat brain tissue was examined. It was found to bind specifically to rat brain crude synaptosomal and membranal preparations. The binding is rapid, displaceable and saturable with a IC50 value of 4 X .000010M. The maximal number of sites is 18 to 25nM/g original tissue in the synaptosomal preparation and only 6 to 8nM/g in the membranal preparation. Scatchard plots of the binding data are not linear, suggesting a heterogenous set of binding sites. Pargyline and a number of neurotransmitters and agonists have only a small effect on desipramine binding; whereas various neurotransmitter antagonists inhibit the binding at the muM concentration range. 24 references. (Author abstract)

**002702** Biggio, G.; Corda, M. G.; De Montis, G.; Stefanini, E.; Gessa, G. L. Institute of Pharmacology, University of Cagliari, Cagliari, Italy **Kainic acid differentiates GABA receptors from benzodiazepine receptors in the rat cerebellum.** Brain Research. 193(2):589-593, 1980.

Intracerebellar injections of kainic acid in male Sprague-Dawley rats markedly decreased (3H)diazepam binding, but increased (3H)GABA binding. These results suggest that cerebellar cortex benzodiazepine receptors are located on structures distinct from those containing sodium dependent GABA receptors. However, the two receptors may coexist in the same structure in other brain areas. 19 references.

**002703** Bigon, E.; Boarato, E.; Bruni, A.; Leon, A.; Toffano, G. Institute of Pharmacology, University of Padova, Largo Meneghetti 2, I-35100 Padova, Italy **Pharmacological effects of phosphatidylserine liposomes: the role of lysophosphatidylserine.** British Journal of Pharmacology. 67(4):611-616, 1979.

Phosphatidylserine depressed brain energy metabolism following intravenous injection into mice in the form of sonicated liposomes, and this effect was enhanced by incubation of the liposomes with rat serum. Similar phosphatidylserine activation was observed after incubation of the phospholipid with purified phospholipase-A2 from pancreas. In both cases, phosphatidylserine was split into the deacylated derivative, lysophosphatidylserine. Lysophosphatidylserine was even more potent than phosphatidylserine in depressing brain energy metabolism, but other lysophospholipids were ineffective. Results indicate that the pharmacological effects of phosphatidylserine liposomes are due to the generation of lysophosphatidylserine. 18 references. (Author abstract modified)

**002704** Blackshear, M. A. U.; Wade, L. H.; Proctor, C. D. Tennessee Neuropsychiatric Institute, 1501 Murfreesboro Road, Nashville, TN 37217 **Effect of crowding on amphetamine-induced disaggregation of brain polyribosomes.** Archives Internationales de Pharmacodynamie et de Therapie. 241(2):180-189, 1979.

The effects of DL-amphetamine on brain polyribosomes were examined in male Sprague-Dawley mice housed in crowded or uncrowded conditions. Although DL-amphetamine (20mg/kg) induced disaggregation of brain polyribosomes 30 minutes after drug administration in both groups, the magnitude of polysome dissociation was greater in crowded animals than in uncrowded mice. The magnitude of polysome dissociation appeared to parallel both the degree of crowding and the intensity of central nervous system stimulation. Haloperidol (1mg/kg) provided protection against amphetamine toxicity in crowded mice. 27 references. (Author abstract modified)

**002705** Blake, James; Tseng, Liang-Fu; Li, Choh Hao. Hormone Research Laboratory, 1088 HSW, University of California, San Francisco, CA 94143 **Synthesis and analgesic activity of human beta-endorphin analogs substituted at positions 17, 18, or 19.** International Journal of Peptide Protein Research. 15:167-170, 1980.

The synthesis and analgesic activity of human beta-endorphin analogs were examined by the tail flick method in mice. Three peptide analogs of beta-endorphine were substituted in positions 17, 18, or 19 and their analgesic potencies measured. The results show that the replacement of Phe-18 or Lys-19 by alanine reduced the potency to 15% whereas the replacement of Leu-17 by alanine reduced the analgesic potency to 68%. It is concluded that the Leu side chain is not as important for the biological activity of of beta-endorphin as are the side chains of Phe and Lys. 18 references. (Author abstract modified)

**002706** Boakes, R. J.; Bradley, P. B.; Candy, J. M. MRC Neuropharmacology Unit, Dept. of Pharmacology, Medical School, Birmingham B15 2TJ, England **Interactions of ()-amphetamine and chlorpromazine on neurones in the lower brain stem of the rat.** British Journal of Pharmacology. 67(2):165-171, 1979.

The ability of chlorpromazine (CPZ) to antagonize the effects of ()-amphetamine on single neurons in the medulla and lower pons of anesthetized male rats was examined. When administered systemically or iontophoretically, CPZ consistently and specifically antagonized the excitatory actions of iontophoretically applied amphetamine, but not of noradrenaline. Amphetamine did not mimic the prolonged inhibitory response of some neurons to noradrenaline, but often excited these neurons; CPZ blocked the excitatory responses to amphetamine. It is concluded that CPZ acts through a presynaptic mechanism to reduce the effect of amphetamine. 23 references. (Author abstract modified)

**002707** Bondy, Stephen C.; Burks, Jack S.; Harrington, Marilyn E. Burks: Neurology Service, Veterans Administration Medical Center, 1055 Clermont Street, Denver, CO 80220 **Uptake and release of putative neurotransmitters: measurements in regions of the normal and Newcastle disease virus-infected mouse brain.** Archives of Neurology. 36(9):540-543, 1979.

The capacity of various regions of the mouse brain to accumulate a series of putative neurotransmitter compounds was studied in cerebral homogenates. This uptake is selective, sodium dependent, energy dependent, and exhibits characteristics of high affinity transport. Calcium stimulated release under depolarizing conditions of accumulated radioactive compounds was also examined. Large regional variations of uptake and release capacity existed. No clear relation between intensity of intake and releasability of transported compounds was seen. The effect of infection of mice with Newcastle disease virus on these processes was investigated. No significant differences were seen in infected mice despite their depressed metabolic rate. 29 references. (Author abstract)

**002708** Borys, Henry K.; Ingall, Glynnis B.; Karler, Ralph. Dept. of Pharmacology, University of Utah College of Medicine, Salt Lake City, UT 84132 **Development of tolerance to the prolongation of hexobarbitone sleeping time caused by cannabidiol.** British Journal of Pharmacology. 67(1):93-101, 1979.

The effects of acute and subacute treatment with cannabidiol (CBD) on hexobarbitone sleeping time and on the hepatic microsomal drug metabolizing system were examined in male ICR mice. A single injection of CBD (120mg/kg i.p.) prolonged sleeping time, but tolerance to this effect developed rapidly when CBD was injected at 24 hour intervals over a 6 day period. Brain hexobarbitone concentration on awakening was unchanged by either treatment. Acute CBD treatment increased the half-time of hexobarbitone in the brain, but the half-time returned to normal with the development of tolerance. Acute CBD treatment also caused a 30% decrease in hepatic cytochrome P-450 level, which returned to normal as tolerance developed. Results suggest that the CBD-induced prolongation of barbiturate sleeping time and the tolerance to this effect are both due to changes in the rate of drug metabolism, which are related to changes in the amount of cytochrome P-450. 23 references. (Author abstract modified)

**002709** Brodde, O.-E.; Gross, G. Institut fur Pharmakologie, Universitat Essen, Hufelandstrasse 55, D-4300 Essen, Germany **(3H)-Spiroperidol labels dopamine receptors in membranes from rabbit mesenteric artery.** Naunyn-Schmiedeberg's Archives of Pharmacology. 311(3):249-254, 1980.

The potent dopamine receptor antagonist (3H)-spiroperidol was used to label binding sites in a membrane fraction derived from rabbit mesenteric artery which had characteristics expected for dopamine receptors. The binding was of high affinity with an equilibrium dissociation constant (KD) of 13.1nM; it was saturable with 110fmol of (3H)-spiroperidol bound/mg protein at maximal occupancy of the sites. Binding at 37 degrees C was rapid and readily reversible. Dopamine receptor antagonists were about 100 to 200 times more potent than alpha-adrenolytic drugs in competing for the (3H)-spiroperidol binding sites and dopamine was much more potent than (-)-noradrenaline, (-)-isoprenaline, clonidine, or serotonin. It is concluded that in a membrane fraction of the rabbit mesenteric artery there exist binding sites for (3H)-spiroperidol indistinguishable from dopamine receptors. Thus, the present results support the view that in vascular smooth muscle there exist specific dopamine receptors. 26 references. (Author abstract modified)

**002710** Brown, D. A.; Constanti, A.; Marsh, S. Dept. of Pharmacology, School of Pharmacy, University of London, 29/39 Brunswick Square, London WC1N 1AX, England **Angiotensin mimics the action of muscarinic agonists on rat sympathetic neurones.** Brain Research. 193(2):614-619, 1980.

Intracellular and extracellular recordings of rat superior cervical ganglia showed that angiotensin-II and muscarine affect the same component of ionic conductance. The two compounds produced qualitatively similar changes in input resistance, membrane slope conductance, and spike activity. Since these postsynaptic effects are mediated by pharmacologically distinct receptors, a common intermediary step or steps may be present. 23 references.

**002711** Brownell, William E.; Manis, Paul B.; Ritz, Louis A. Dept. of Neuroscience, Box J-244, JHMHC, University of Florida, Gainesville, FL 32610 **Ipsilateral inhibitory responses in the cat lateral superior olive.** Brain Research. 177(1):189-193, 1979.

Ipsilateral excitatory and contralateral inhibitory responses of units in the lateral superior olive (LSO) of unanesthetized, decerebrate cats were examined. These units displayed robust spontaneous activity, and showed inhibitory sidebands in response to ipsilateral ear stimulation. Spontaneous activity and ipsilateral inhibitory sidebands were not evident in cats treated with an anesthetic dose of sodium pentobarbital. 16 references.

**002712** Brus, R.; Herman, Z. S.; Szkilnik, R.; Zabawska, J. Dept. of Pharmacology, Biological-Physiological Institute of the Silesian School of Medicine/Katowice, Marksa 38, 41-808 Zabrze, Poland **Mediation of central prostaglandin effects by serotonergic neurons.** Psychopharmacology. 64(1):113-120, 1979.

The possible involvement of the prostaglandins (PGs) in the function of the central serotonergic system was examined in rats pretreated with 5,6-dihydroxytryptamine, which causes degeneration of central serotonergic neurons. Depressive behavioral effects of PGF2alpha and PGE2 were evidently inhibited at 10 days posttreatment. Central chemical serotoninectomy abolished the hyperthermic and hypertensive effects of PGF2alpha, but only slightly affected those of PGE2. It is concluded that serotonergic neurons mediate the depressive behavioral action of both PGs. They also mediate the hyperthermic and hypertensive action of PGF2alpha, but not PGE2. This latter result suggests that these PGs have different central modes of action. 33 references. (Author abstract modified)

**002713** Buckman, Trent; Eiduson, Samuel. Eiduson: Neuropsychiatric Institute, 760 Westwood Plaza, Los Angeles, CA 90024 **Studies of pargyline-monoamine oxidase binding using a spin label probe analog.** Journal of Neurochemistry. 34(6):1594-1602, 1980.

Analogs of the monoamine oxidase (MAO) inhibitor pargyline with a nitroxide free radical moiety attached through an ether linkage to the para position on the benzene ring have been prepared and reacted with solubilized MAO preparations from rat and beef brain and pig liver. These compounds behave as normal irreversible inhibitors of catalytic activity, with some preference for B-type enzyme. When the reaction was monitored by electron spin resonance (ESR), line broadening effects indicative of binding and with an apparent relation to substrate specificity of the preparation were observed. In addition, there was a slow decrease in intensity of the ESR spectra, which could be retarded by the addition of other MAO inhibitors or increased O2, and enhanced by flavin reduction. It appears to be related to development of the irreversible phase of MAO inhibition. Signal recovery with added O2, and studies of a model reaction with free flavin, suggest the signal loss to be a line broadening effect due to interaction with an enzyme generated paramagnetic species rather than to direct reduction of the nitroxide radical. 17 references. (Author abstract)

**002714** Burkard, W. P. Pharmaceutical Research Dept., F. Hoffman-La Roche & Co., Ltd., CH-4002 Basel, Switzerland **Specific binding sites in rat brain for a new and potent inhibitor of 5-hydroxytryptamine uptake: Ro 11-2465.** European Journal of Pharmacology. 61(4):409-410, 1980.

The binding of the 5-hydroxytryptamine (5-HT) uptake inhibitor Ro 11-2465 to male rat brain membranes was examined. Scatchard plots revealed the presence of two binding components, of high and low affinity. The potency of a series of compounds in inhibiting 3H-Ro 11-2465 binding corresponded to the drugs' potencies as inhibitors of 5-HT uptake. 5 references.

**002715** Burns, Leslie Lee. University of Illinois at the Medical Center **Pattern analysis of neuronal firing in feline thalamus: the effect of sleep, food reward and opiates. (Ph.D. dissertation).** Dissertation Abstracts International. 40(3):4245-B, 1980. Ann Arbor, Univ. Microfilms No. 8007286, 165p., 1979.

The effects of sleep, food reward, and opiates on single unit neuronal firing in feline thalamus were investigated via a newly developed pattern analysis technique. The pattern analysis utilized inequality testing to determine if detected patterning differs from expected frequencies of an independent stochastic model. Results indicate that patterned activity is associated with more attentive states (desynchronized) and a reduction of patterns is associated with inattentive states (synchronized quiet wakefulness). Food reinforced bar-pressing behaviors was also studied in this manner, and it was found that there is a reduction of patterns during the synchronized elctrocorticogram phase following reinforcement. It is concluded that the effect of an injection of morphine on cells in the centromedian parafascicularis area is to lock the cells into a particular specific firing pattern which does not vary. (Journal abstract modified)

**002716** Bus Lassen, J.; Lund, J.; Bechgaard, E.; Sondergaard, I. A/S Ferrosan, Dept. of Pharmacology, Sydmarken 1-5, DK-2860 Soeborg, Denmark **Inhibition of 5-HT uptake into neurons and platelets in mice treated chronically with chlorimipramine and femoxetine.** Psychopharmacology. 64(2):149-153, 1979.

The effect of nialamide, a monoamine oxidase inhibitor known to potentiate hypermotility, on motility was studied in mice after 4 weeks of feeding with a normal diet and diets containing various concentrations of the 5-hydroxytryptophan (5-HT) uptake inhibitors chlorimipramine and femoxetine. Chronic treatment with the two substances enhanced the motor effects of nialimide about equally, which indicates a preservation of the neuronal 5-HT uptake inhibition during such treatment. The effect of the two drugs was obtained at plasma levels equivalent to or lower than the steady-state plasma concentrations found in patients treated with chlorimipramine or femoxetine. Determination of decreased blood 5-HT after treatment was used as an in vivo test for inhibition of 5-HT uptake into platelets. Femoxetine was a much weaker depletor of blood 5-HT than chlorimipramine. These results indicate that blockade of neuronal 5-HT than chlorimipramine. These results indicate that blockade of neuronal 5-HT uptake is obtained at lower doses of femoxetine than blockade of 5-HT uptake into platelets. In contrast, chlorimipramine presumably inhibits 5-HT uptake into neurons and platelets at about the same dose. 28 references. (Author abstract modified)

**002717** Buzsaki, G.; Kellenyi, L.; Grastyan, E. Institute of Physiology, University Medical School, H-7643 Pecs, Hungary **Effects of scopolamine upon hippocampal electrical activity associated with running and swimming in rats.** Physiology & Behavior. 24(1):191-194, 1980.

The quantitative effects of scopolamine hydrobromide (5 to 10mg/kg i.p.) on hippocampal rhythmic slow activity (RSA) were studied in rats with implanted hippocampal electrodes during running and swimming. Scopolamine caused a significant upward frequency shift of RSA during these behaviors. Thus, anticholinergic treatment did not abolish the hippocampal RSA associated with movement, but significantly altered its frequency distribution pattern. 12 references. (Author abstract modified)

**002718** Bylund, David B.; Martinez, J. Ricardo. Dept. of Pharmacology, University of Missouri, School of Medicine, Columbia, MO 65212 **Alpha2-adrenergic receptors appear in rat salivary glands after reserpine treatment.** Nature. 285(5762):229-230, 1980.

The alpha2 adrenergic receptors in the submandibular gland of control and reserpine treated rats were characterized using the radioligand, 3H-clonidine. In previous studies, alpha1 adrenergic receptors, but not alpha2 adrenergic receptors have been identified in rat submandibular gland. Results indicate that a single treatment of reserpine results in the appearance of alpha2 adrenergic binding sites within 12 hours. Continued treatment with the drug produces further increases in the number of alpha2 adrenergic receptors, such that after 7 days the levels of alpha1 and alpha2 adrenergic receptors are similar. It is noted that this is the first example of drug treatment resulting in the appearance of a receptor type which was not previously detectable. 13 references. (Author abstract modified)

**002719** Carrer, Hugo F.; Ferreyra, Horacio. Instituto de Investigacion Medica, Mercedes y Martin Ferreyra, Casilla de Correo 389, 5000 Cordoba, Argentina **Anesthetic-dependent excitability changes in the hypothalamic ventromedial nucleus of the rat.** Experimental Neurology. 67(3):524-538, 1980.

The effects of urethane and pentobarbital anesthesia on the responses of ventromedial hypothalamic (VMH) neurons to amygdaloid stimulation were examined in rats. Results indicate that VMH neurons receive both inhibitory and excitatory influences from the amygdala. The excitatory influence was predominant in awake or urethane anesthetized animals, but a GABA mediated inhibitory influence was observed under pentobarbital anesthesia. 37 references. (Author abstract modified)

**002720** Cassens, Geraldine; Kuruc, Alvin; Orsulak, Paul J.; Schildkraut, Joseph J. Neuropsychopharmacology Laboratory, Massachusetts Mental Health Center, 74 Fenwood Road, Boston, MA 02115 **Amphetamine withdrawal: effects on brain levels of MHPG-SO4 in the rat.** Communications in Psychopharmacology. 3(4):217-223, 1979.

The effects of chronic administration of and withdrawal from d-amphetamine on brain levels of 3-methoxy-4-hydroxy-phen-

ylglycol sulfate (MHPG-SO4) in the rat were investigated. Although acute administration of d-amphetamine increases levels of MHPG-SO4 (a major metabolite of norepinephrine), chronic administration of a fixed dose of d-amphetamine produced tolerance to the amphetamine-induced increase in brain levels of MHPG-SO4. Moreover, after withdrawal from chronic escalating doses of d-amphetamine, significant decrease in brain levels of MHPG-SO4 were observed 24 or 48 hours after the last dose of d-amphetamine. The decreases in levels of MHPG-SO4 in rat brain may be analogous to the decreases in the urinary excretion of MHPG that have been observed clinically in man during the depressions that occur following withdrawal from large doses of amphetamine. 26 references. (Author abstract modified)

**002721** Catapane, Edward J.; Collins, Erica D.; Marcano, Juan A.; Stefano, George B. Dept. of Natural Sciences, Medgar Evers College, CUNY, Brooklyn, NY 11225 **Denervation produces supersensitivity of a serotonergically innervated structure.** European Journal of Pharmacology. 62(1):111-115, 1980.

The lateral ciliated gill epithelium of the marme mollusc Mytilus edulis was denervated physically or chemically (with 5,6-dihydroxytryptamine). Both treatments caused a supersensitive response of the lateral ciliated cells to the excitatory effects of superfused serotonin. Endogenous serotonin levels were reduced by both treatments. 10 references. (Author abstract modified)

**002722** Cho, Tae Mook. University of California, San Francisco **Mechanisms of opiate-receptor interactions. (Ph.D. dissertation).** Dissertation Abstracts International. 40(7):3109-B, 1980. Ann Arbor, Univ. Microfilms No. 8001346, 157p., 1978.

The pharmacological effects of opiate agonists and antagonists, and the structure activity relationships are analyzed to establish a reasonable molecular mechanism of their actions which could account for the observed effects and provide a basis for search for the receptor. Based on the availability of opiates at the receptor site and the ionic nature of the drug receptor complex, a molecular mechanism of opiate agonist and antagonist actions is proposed. The proposed theory is tested using cerebroside sulfate (CS) as a model opiate receptor. Detailed observations and discussions which support the proposed theory are presented. (Journal abstract modified)

**002723** Chuang, D.-M.; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Beta-adrenergic receptors of frog erythrocytes: biochemical sequelae following stimulation with isoproterenol.** Neurochemical Research. 4(6):777-793, 1979.

Biochemical sequelae following stimulation with isoproterenol of beta-adrenergic receptors of frog erythrocytes were examined. The cyclic adenosine 3',5'-monophosphate (cAMP) dependent protein kinase was activated for several hours following stimulation. This activation outlasted the duration of the increase of cAMP content. Following a persistant stimulation of beta-adrenergic receptors with isoproterenol, the phosphorylation of selective membrane proteins was increased. This increase in phosphorylation lasted longer than 4 hours but less than 12 hours. Between 2 and 4 hours after receptor stimulation, the loss of beta-adrenergic receptor from plasma membrane was maximal, and the phosphorylation of two membrane proteins characterized by molecular weights of 60,000 and 38,000 daltons was selectively enhanced. In addition it was noted that isolated erythrocytes are capable of synthesizing RNA and polypeptides and that incubation with (-)-isoproterenol induces a long-term delayed increase of the synthesis of erythrocyte proteins. This increase in the synthesis of proteins appears to require new RNA synthesis. Thus, the possibility can be entertained that this delayed increase in protein synthesis participates in the new synthesis of receptor and is operative in the termination of beta-adrenergic receptor subsensitivity elicited by a persistent stimulation with (-)-isoproterenol. 24 references. (Authorabstract modified)

**002724** Cicero, Theodore J. Dept. of Psychiatry, Washington University School of Medicine, St. Louis, MO 63110 **Effects of exogenous and endogenous opiates on the hypothalamic-pituitary-gonadal axis in the male.** Federation Proceedings. 39(8):2551-2554, 1980.

The effects of opiate drugs on the hypothalamic pituitary gonadal (H-P-G) axis in the male and the role of endogenous opioids in regulating activity in this axis are reviewed. The currently available evidence indicates that narcortics do not affect the catabolism of testoterone by the liver or testicular steroidogenesis. The data favor a direct action of the hypothalamic pituitary luteinizing hormone (LH) axis, probably by inhibiting the secretion of LH releasing hormones from the hypothalamus. The effects of narcotics on serum LH appear to be mediated via specific opioid receptors, suggesting that a naturally occuring opioid-like substance exists that normally inhibits LH. It is concluded that opiate drugs inhibit the function of the H-P-G axis by occupying opiate receptors in the hypothalamus and that opioids exist that normally bind to these receptors and regulate activity in this axis. 26 references. (Author abstract modified)

**002725** Collins, G. G. S. Dept. of Pharmacology, University of Sheffield, Sheffield S10 2TN, England **Release of endogenous amino acid neurotransmitter candidates from rat olfactory cortex slices: possible regulatory mechanisms and the effects of pentobarbitone.** Brain Research. 190(2):517-528, 1980.

The effects of pentobarbitone on the release of amino acid transmitter candidates (aspartate, GABA, and taurine) from rat olfactory cortex slices were examiend. Release of aspartate, the presumed excitatory transmitter of some of the lateral olfactory tract fibers, is reduced by muscimol and this effect is antagonized by picrotoxin. Low concentrations of pentobarbitone also reduce aspartate release, but this effect is picrotoxin-insensitive. Pentobarbitone significantly increases release of GABA when slices are synaptically activated although the mechanism of this effect is unclear. It is suggested that GABA release may be regulated by presynaptic autoreceptors. 45 references. (Author abstract modified)

**002726** Consolo, S.; Forloni, G. L.; Garattini, S.; Ladinsky, H.; Tirelli, A. S. Istituto di Ricerche Farmacologiche Eritrea, 62-20157 Milan, Italy **Differential effects of the isomers of fenfluramine and norfenfluramine on rat striatal acetylcholine content.** Journal of Pharmacy and Pharmacology. 31(10):706, 1979.

The effects of the optical isomers of fenfluramine and norfenfluramine on striatal acetylcholine (ACh) were determined in female CD-COBS rats. Results showed that ()-norfenfluramine was the most active compound in increasing striatal ACh, followed by ()-fenfluramine and (-)-norfenfluramine; (-)-fenfluramine was inactive. The possible involvement of serotonergic and dopaminergic mechanisms in these drug actions is discussed. 8 references.

**002727** Corcoran, Michael E.; Mason, Stephen T. Dept. of Psychology, University of Victoria, P.O. Box 1700, Victoria, B.C. V8W 2Y2, Canada **Role of forebrain catecholamines in amygdaloid kindling.** Brain Research. 190(2):473-484, 1980.

The rate and pattern of seizure development provoked by repeated electrical stimulation of the amygdala (kindling) was assessed in rats that had been pretreated with intracerebral injections of the selective catecholaminergic neurotoxin 6-hydroxydopamine. Rats with selective depletion of forebrain noradrena-

line displayed a highly significant facilitation of both primary site and secondary-site kindling, whereas no such effect occurred in rats with selective depletion of forebrain dopamine. The facilitative effects of noradrenaline depletion were apparently related to disinhibition of the spread of seizure discharge from the stimulated site rather than to increased epileptogenicity in the stimulated site itself. It is concluded that these results are consistent with previous evidence that noradrenaline reduces the susceptibility of the central nervous system to epileptiform activity, and they suggest that a lessening of seizure suppressant nonadrenergic function in the forebrain might be part of the mechanism underlying kindling. 40 references. (Author abstract)

**002728** Corda, M. G.; Biggio, G.; Gessa, G. L. Institute of Pharmacology, University of Cagliari, Cagliari, Italy **Brain nucleotides in naive and handling-habituated rats: differences in levels and drug-sensitivity.** Brain Research. 188(1):287-290, 1980.

Striatal cyclic AMP levels and cerebeller cyclic GMP levels in naive male Sprague-Dawley rats killed by microwave irradiation were markedly higher than those in rats habituated to the handling maneuvers preceding sacrifice. Dopamine receptor agonists and antagonists and GABAergic drugs also had differential effects in naive and handling habituated animals. These findings indicate that nigrostriatal dopaminergic and cerebeller GABAergic transmission play an important role in the response to handling stress and suggest that handling habituated rats may be a more sensitive model than naive rats for studying drugs that act on striatal dopamine receptors. 10 references.

**002729** Corrigall, W. A.; Linseman, M. A. Neurobiology Section, Addiction Research Foundation, Toronto, Ontario, Canada **A specific effect of morphine on evoked activity in the rat hippocampal slice.** Brain Research. 192(1):227-238, 1980.

The effect of morphine on CA1 field potential in the transverse hippocampal slice was examined. Morphine consistently produced an augmentation of evoked activity manifest as: 1) a decrease in the threshold for generation of a population spike and, 2) generation of an additional population spike (s) whose amplitude was proportional to the position of the sampled response on its input/output curve. Both of these opiate effects were stereospecific and naloxone reversible. Additional population spikes occurred in opiate medium with either orthodromic or antidromic activation of the pyramidal cells, and the antidromic effect was abolished when synaptic transmission was blocked, suggesting that morphine did not act directly upon the pyramidal cells. Recordings of population excitatory postsynaptic potentials in the dendrites of the pyramidal cells showed no changes due to opiate exposure near threshold. Opiate effects were mimicked by the gamma-aminobutyric acid (GABA) antagonist picrotoxin, and were partially to fully reversed by GABA itself, suggesting that disinhibition of pyramidal cells might be involved as a mechanism in this opiate effect. The data are evidence for a specific primary effect of morphine within the hippocampus in spite of the low numbers of opiate receptors in this brain region. 23 references. (Author abstract)

**002730** Cox, B.; Lee, T. F. Dept. of Pharmacology, Materia Medica and Therapeutics, Stopford Building, Manchester University, Manchester M13 9PT, England **Evidence for an endogenous dopamine-mediated hypothermia in the rat.** British Journal of Pharmacology. 67(4):605-610, 1979.

Unilateral intrahypothalamic injection of dopamine (10mcg) or amphetamine (10mcg) caused a fall in core temperature in male Sprague-Dawley rats. Pimozide (0.5mg/kg i.p.) significantly reduced the hypothermic response, but phentolamine (1mg/kg i.p.) and methsergide (5mg/kg i.p.) were ineffective. Systemic pretreatment with cocaine (20mg/kg) abolished the hypothermic effect of amphetamine, but slightly enhanced the hypothermic response to dopamine. Systemic pretreatment with tranylcypromine (10mg/kg) had no significant effect on the hypothermia induced by amphetamine of dopamine. Cocaine and tranylcypormine (i.p.) both caused a fall in core temperature, which was significantly antagonized by systemic or central pretreatment with pimozide but not by phentolamine or methysergide. Unilateral intrahypothalamic injection of cocaine (20mcg) or tranylcypromine (10mcg) also caused a significant fall in core temperature, which was reduced by intrahypothalamic pretreatment with pimozide but not phentolamine or methysergide. Results suggest that a dopaminergic system within the preoptic region mediates the lowering of core temperature in rats. 21 references. (Author abstract modified)

**002731** Crosby, G.; Tannebaum, A.; Sokoloff, L. Laboratory of Cerebral Metabolism, NIMH, Bethesda, MD 20205 **Ketamine alters regional glucose utilization in rat brain. (Unpublished paper).** Bethesda, MD, NIMH, 1980. 1 p.

The first quantitative measurement of regional cerebral glucose utilization (CMRG) following ketamine administration is reported. The data establish that ketamine has effects in limbic and auditory structures. Unlike previous reports, changes in cortical CMRG, which suggest auditory and somatosensory deprivation, are noted. The visual cortex was stimulated along with the basal ganglia, a finding consistent with behavioral observations and reports indicating that ketamine increases dopamine turnover in rat brain. The implications of changes found in white matter are discussed. It is suggested that ketamine may act through binding on a PCP receptor to produce changes in dopamine or other neurotransmitter levels. The anesthetic action of ketamine may result from decreased auditory and somatosensory input while the stimulation of the visual cortex could explain the visual hallucinations which patients sometimes report after this drug. 7 references. (Author abstract modified)

**002732** Dafny, N.; Brown, M.; Burks, T. F.; Rigor, B. M. Dept. of Neurobiology, University of Texas Medical School, Houston, TX 77025 **Patterns of unit responses to incremental doses of morphine in central gray, reticular formation, medial thalamus, caudate nucleus, hypothalamus, septum and hippocampus in unanesthetized rats.** Nw Neuropharmacoloy. 18(5):489-495, 1979.

Freely moving, unanesthetized male Sprague-Dawley rats implanted stereotaxically with electrodes in the central gray, mesencephalic reticular formation, medial thalamus, caudate nucleus, anterior and ventromedial hypothalamus, lateral septum, and dorsal hippocampus were injected with incremental doses of morphine (0.5, 1.0, 5.0, 10.0, and 30.0mg/kg i.p.) followed by naloxone (1.0mg/kg i.p.). Spontaneous multiunit activity was recorded from all eight brain sites, and data were used to classify patterns of drug response for each region. Results indicate that each structure has its own pattern of response to morphine and naloxone. These electrophysiological findings are discussed in relation to previous neurochemical studies of regional opiate binding and brain function. 28 references. (Author abstract modified)

**002733** Dafny, Nachum. Dept. of Neurobiology and Anatomy, University of Texas Medical School, Houston, TX 77025 **Multiunit recording from medial basal hypothalamus following acute and chronic morphine treatment.** Brain Research. 190(2):584-592, 1980.

Physiological responses were observed from multiunit recordings from the medial basal hypothalamus (MBH) of unanesthetized, freely moving Sprague-Dawley rats following acute and chronic morphine treatment. Five patterns of electrical activity

were identified in the MBH with relation to morphine and naloxone: 1) monophasic increases in neuronal activity following morphine, 2) monophasic decreases in neuronal activity, 3) biphasic patterns of response, 4) no response to morphine but alteration in electrical discharges after naloxone, and 5) multiunits which failed to change their firing rate with any treatment. It is concluded that the variety of response patterns within the MBH indicates that morphine and naloxone caused different effects on different cell types. 32 references.

**002734** de Boer, Th.; Stoof, J. C.; van Duyn, H. Dept. of Neurology, Medical Faculty, Free University, Van der Boechorststraat 7, 1007 MC Amsterdam, The Netherlands **Effect of penicillin on transmitter release from rat cortical tissue.** Brain Research. 192(1):296-300, 1980.

The release of GABA and several other neurotransmitters from rat cortical tissue following application of penicillin was investigated in male albino rats. The principal finding is that penicillin does not selectively affect the GABAergic system, but also several other neuronal systems presynaptically. An almost complete blockade of the release of the four transmitters studied (GABA, glutamate, acetylcholine, noradrenaline) was observed with 34 mM penicillin. Apart from the apparent lack of specificity, concentrations of 34mM penicillin seem to be supramaximal for its epileptogenic effects since both in vitro and in vivo epileptogenesis has been described to occur in a concentration range of 0.5 to 8.5 mM penicillin. Since the presynaptic effects of penicillin were not restricted to the GABAergic system, these results do not allow the inference of a causal relationship between (3H)GABA release inhibition and the epileptogenic effects of penicillin. 26 references.

**002735** Delanoy, Richard L., Jr. University of Florida **Peptide hormone interactions with brain catecholamine metabolism. (Ph.D. dissertation).** Dissertation Abstracts International. 41(1):397-B, 1980. Ann Arbor, Univ. Microfilms No. 8016523, 133p., 1979.

The accumulation of (3H) catecholamines from (3H)tyrosine in frontal cortical, septal, striatal and hippocampal slices was examined following intracerebroventricular injections of ACTH1-24, lysine vasopressin (LVP) and saline. Both ACTH1-24 and LVP selectively increased the accumulation of (3H)dopamine (DA) in frontal cortical slices but did not affect (3H)norepinephrine (NE) accumulation. LVP also inhibited the accumulation of (3H)DA in striatal slices. The selective activation of the mesocortical DA system by intracerebroventricular injections of peptides which also occurs in response to footshock stress suggests that endogenous ACTH and/or LVP may mediate the stress-induced mesocortical DA activation. Control experiments performed to characterize the normal kinetics and the effects of elevated K, apomorphine, and haloperidol on catecholamine synthesis are described. (Journal abstract modified)

**002736** Dembiec, Dorothy. Dept. of Neurology, Mount Sinai School of Medicine, Fifth Avenue and 100 St., New York, NY 10029 **Inhibition of potassium-stimulated release of (3H)dopamine from rat striata as a result of prior exposure to cocaine, nomifensine, or mazindol.** Neurochemical Research. 5(3):345-349, 1980.

Inhibition of potassium-stimulated release of (3H)dopamine from rat striata as a result of prior exposure to cocaine, nomifensine, or mazindol was studied. The nerve terminals in the striata of rat brain were labeled in vitro with (3H)dopamine via the uptake mechanism for catecholamines. Subsequently, the striata were incubated with cocaine, nomifensine, or mazindol, inhibitors of cathecholamine uptake. The tissues were rinsed in fresh medium and then stimulated with 20mM potassium to induce release of (3H)dopamine. Under these conditions, it is reported, each drug decreased the pottasium stimulated release of radioactivity by 40 to 50% compared to control tissues which had not been exposed to the drugs. 13 references. (Author abstract modified)

**002737** Devoto, Paola; Marchisio, Anna Maria; Carboni, Ezio; Spano, Pier Franco. Spano: Institute of Pharmacology and Pharmacognosy, Viale Diaz 182, I-09100 Cagliari, Italy **Detection of 3H-cimetidine specific binding in rat anterior pituitary.** European Journal of Pharmacology. 63(1):91-93, 1980.

The binding of 3H-cimetidine, a potent H2-receptor antagonist, was demonstrated in anterior pituitary membrane preparations from male Sprague-Dawley rats. Scatchard analysis revealed a single binding component, with a dissociation constant of 40.3nM and a maximal binding capacity of 1.94pmoles/mg protein. Histamine and the alpha-adrenergic blocking agent phentolamine were more than 1000 and 250 times, respectively, less potent than the H2-antagonists cimetidine and metiamide in displacing 3H-cimetidine binding. The H1-antagonists mepyramine and promethazine failed to inhibit specific binding, as did desmethylimipramine, dopamine, and propranolol. It is suggested that H2-receptors on pituitary lactotrophs may be involved in the prolactin releasing effect of cimetidine in humans. 5 references.

**002738** Di Chiara, G.; Morelli, M.; Porceddu, M. L.; Mulas, M.; Del Fiacco, M. Institute of Pharmacology, University of Cagliari, Cagliari, Italy **Effect of discrete kainic acid-induced lesions of corpus caudatus and globus pallidus on glutamic acid decarboxylase of rat substantia nigra.** Brain Research. 189(1):193-208, 1980.

To clarify the role of the globus pallidus as a source of nigral GABA terminals, kainic acid was used to destroy pallidal perikarya without damaging axons en passage. Kainic acid produced a loss of neuronal perikarya and reactive gliosis in the globus pallidus. Large multipolar neurons of the globus pallidus were destroyed on the lesioned side. Lesions of the pallidum caused a 5.5% reduction of nigral glutamate decarboxylase (GAD) activity. Lesions restricted to the head of the caudate caused a 19% drop in nigral GAD, and lesions of the caudate body caused a 53% reduction. Lesions of the caudate tail had no effect. Results indicate that nigral GAD arises mostly from the body but partially from the head of the caudate. 31 references. (Author abstract modified)

**002739** Divakaran, P.; Joiner, F.; Rigor, B. M.; Wiggins, R. C. Wiggins: Dept. of Neurobiology and Anatomy, University of Texas Medical School at Houston, P. O. Box 20708, Houston, TX 77025 **Accumulation and persistence of halothane in adult and fetal rat brain as a result of subanesthetic exposure.** Journal of Neurochemistry. 34(6):1543-1546, 1980.

The accumulation and persistence of halothane in fetal and maternal rat brain as a result of subanesthetic exposure were investigated. The concentration of halothane employed (0.5%) was well below the anesthetic range (1% to 2%) and much greater than the trace (1 to 10 ppm) levels typically found in operating rooms. Results indicate that: 1) halothane accumulation in adult brain is 20% to 30% more rapid than in adult liver, fetal brain, or fetal body; 2) after several hours of exposure, the concentration of halothane in fetal tissues is essentially the same as in maternal brain and liver; and 3) all tissue values decreased by about 50% within 3 hr after last exposure, and had, on average, fallen below the detection limit within 24 hr after the last exposure. Thus, neither the interposition of a placenta between the two circulatory systems, nor the absence of detoxification capability in fetal liver has any significant effect on fetal halothane accumulation or retention. 35 references.

**002740** Dolphin, A.; Hamont, M.; Bockaert, J. Bockaert: Laboratoire de Physiologie Cellulaire, Groupe N.B., 11 place Marcellin Berthelot, F-75231 Paris Cedex 05, France **The resolution of dopamine and beta1- and beta2-adrenergic-sensitive adenylate cyclase activities in homogenates of cat cerebellum, hippocampus and cerebral cortex.** Brain Research. 179(2):305-317, 1979.

The stimulation of adenylate cyclase by dopamine and various beta-adrenergic agonists was examined in homogenates from cat cerebral cortex, cerebellum, and hippocampus. The relative potencies of the beta1-antagonist practolol and the beta2-antagonist butoxamine in blocking the stimulation of adenylate cyclase in these three regions was also examined. Results indicate that a beta2-adrenergic receptor is coupled to adenylate cyclase in the cerebellum, whereas beta1-adrenergic receptors are coupled to the enzyme in the cortex and hippocampus. This conclusion was further substantiated by comparison of the affinities of a series of beta-adrenergic agonists and antagonists for brain beta-adrenergic receptors subtypes with those receptors previously characterized in lung and heart. 21 references. (Author abstract modified)

**002741** Drouva, Sophia V.; Epelbaum, Jacques; Tapia-Arancibia, Lucia; Laplante, Eliane; Kordon, Claude. Unite 159 de Neuroendocrinologie, Centre Paul Broca de l'INSERM, 2ter rue d'Alesia, 75014 Paris, France **Met-enkephalin inhibition of K-induced LHRH and SRIF release from rat mediobasal hypothalamic slices.** European Journal of Pharmacology. 61(4):411-412, 1980.

Methionine-enkephalin (MET) and naloxone (NAL) both failed to alter the spontaneous release of luteinizing hormone releasing hormone (LHRH) or somatostatin (SRIF) in slices of the male Wistar rat mediobasal hypothalamus. However, MET significantly inhibited the release of LHRH and SRIF induced by potassium depolarization. Nalozone had no direct effect on the potassium evoked release of the neuropeptides, but did completely reverse the inhibitory effect of MET. Results suggest that endogenous opiates act through specific opiate receptors localized on LHRH and SRIF neurons to modulate the release of neurohormones. This interaction may account for the changes in plasma luteinizing hormone and growth hormone levels observed after opiate administration. 5 references.

**002742** Drucker-Colin, Rene; Espejel, Rosa Maria. Centro de Investigaciones en Fisiologia Celular, Universidad Nacional Autonoma de Mexico, Apartado Postal 70-600, Mexico 20, D.F. **Chronic administration of chloramphenicol, a protein synthesis inhibitor, selectively decreases REM sleep.** Behavioral and Neural Biology. 29(3):410-413, 1980.

The effects of chronic administration of chloramphenicol on REM sleep were examined in 12 cats. Following a 12 hour baseline recording period, each cat was administered 100mg/kg of chloramphenicol orally for 12 consecutive days. Six of the cats were given no drug on Day 10, in order to determine the effects of withdrawal. Results indicated that there was a specific decrease of REM on each of the 12 chloramphenicol days, except for Day 10. There were no changes in either wakefulness or slow wave sleep. It was also observed that the decrease of REM was the result of a decrease in the frequency of REM periods, rather than in the duration of individual periods. It was additionally observed that there was no rebound of REM sleep upon withdrawal of chloramphenicol. The results further support the idea that protein molecules particpate in REM sleep triggering mechanisms. 10 references. (Author abstract)

**002743** Duggan, A. W.; Griersmith, B. T. Dept. of Pharmacology, John Curtin School of Medical Research, Australian National University, Canberra, Australia **Methyl xanthines, adenosine 3',5'-cyclic monophosphate and the spinal transmission of nociceptive information.** British Journal of Pharmacology. 67(1):51-57, 1979.

When administered from micropipettes in the substantia gelatinosa, cyclic AMP, its butyryl derivatives, and the methyl xanthines theophylline and isobutyl methyl xanthine (IBMX) had no effect on the excitation of neurons of spinal laminae IV and V by noxious heating of the skin or deflection of hairs in anesthetized spinal cats. Electrophoretic applications of morphine reduced the responses of these cells, and the morphine effect was not modified by cyclic AMP or the methyl xanthines. Intravenously administered IBMX produced large transient increases in the firing rate of C-fibers and in the excitation of dorsal horn neurons by noxious heating of the skin. When dorsal horn neurons were activated by electrical stimulation of the tibial nerve with a stimulus adequate to excite C-fibers, intravenous IBMX produced a small increase or no increase in the number of spikes per stimulus. These findings suggest that inhibition of cyclic AMP synthesis is not relevant to the analegesic action of morphine in cats. 20 references. (Author abstract modified)

**002744** Dupont, Andre; Barden, Nicholas; Cusan, Lionel; Merand, Yves; Labrie, Fernand; Vaudry, Hubert. Laboratoire d'Endocrinologie Moleculaire, Le Centre Hospitalier de l'Universite Laval, Quebec G1V 4G2, Canada **Beta-endorphin and Met-enkephalins: their distribution, modulation by estrogens and haloperidol, and role in neuroendocrine control.** Federation Proceedings. 39(8):2544-2550, 1980.

The changes of pituitary hormone release induced by beta-endorphin and Met-enkephalin and the influences of treatment with estrogens on the Met-enkephalin content of discrete brain nuclei in the rat were examined. A single dose of beta-endorphin injected in unanesthetized male rats led to a sevenfold stimulation of plasma prolactin (PRL) levels 10 to 20 min after injection of the peptide, while a dose of 2mcg of beta-endorphin led to a comparable stimulation of plasma growth hormone (GH) concentration. Met-enkephalin was much less potent than beta-endorphin in stimulating PRL and GH release. Naloxone, a specific opiate antagonist, completely blocked the stimulation of GH and PRL release. Treatment with both estrogens and haloperidol led to differential effects on Met-enkephalin content in various brain nuclei. 53 references. (Author abstract modified)

**002745** Ebel, A.; Durkin, T.; Ayad, G.; Mack, G.; Mandel, P. Centre de Neurochimie du CNRS, 11, rue Humann, F-67085 Strasbourg Cedex, France **Genetically determined cholinergic involvement in morphine-induced behavioural responses in mice.** Neuropharmacology. 19(5):423-427, 1980.

Choline acetyltransferase (CAT) activities were measured in several brain regions of two inbred strains of mice which differ in their reaction to opiates. CAT activity was significantly decreased in the corpus striatum of C57BL/6J mice, which show locomotor hyperactivity after morphine treatment. Morphine depresses motor activity in DBA/2J mice, but did not alter CAT activity. It is suggested that the decreased striatal CAT activity in C57BL/6J mice reflects an imbalance of the striatal dopaminergic/cholinergic equilibrium required for normal motor function. 53 references. (Author abstract modified)

**002746** Egashira, Toru; Kamijo, Kazuya. Dept. of Pharmacology, Medical College of Oita, Toi, Hazama-cho, Oita 879-55, Japan **Synthetic rates of monoamine oxidase in rat liver after clorgyline or deprenyl administration.** Japanese Journal of Pharmacology. 29(4):677-680, 1979.

The recovery of type-A and type-B monoamine oxidase (MAO) activity was studied in male Wistar rat liver microsomes

and mitochondria following treatment with clorgyline or deprenyl. Results showed that MAO activity in the liver gradually returned to normal and that the recovery of type-A activity was slower than that of type-B activity. These findings suggest that MAO activity in the brain and heart is also likely to recover following treatment with MAO inhibitors. 13 references.

002747 Ehlers, C. L.; Killam, E. K. Dept. of Anatomy, UCLA School of Medicine, Los Angeles, CA 90024 **The influence of cortisone on EEG and seizure activity in the baboon, Papio papio.** Electroencephalography and Clinical Neurophysiology. 47(4):404-410, 1979.

The ability of cortisone to modify EEG and seizure activity was investigated in 4 baboons, Papio papio. Acute intramuscular doses (0.5 to 4mg/kg) caused a dose dependent increase in seizure response to a flashing light stimulus which was apparent in both seizure duration and the spread of convulsive activity. Along with enhancement of seizures, cortisone was found to cause marked changes in the EEG, ranging from the appearance of interictal paroxysmal activity to alterations in spectral characteristics of the wave forms. Increases in slow waves appeared concomitant with a decrease in fast activity in the 18 to 25 c/sec range. Since previous studies have shown that seizure proclivity is maximal at the time of day when cortisol excretion rates peak, these findings lend further support to the idea that corticosteroids may be involved in the rhythmic variation of seizure activity in the baboon. 18 references. (Author abstract)

002748 Ehlert, Frederick J.; Yamamura, Henry I.; Triggle, David J.; Roeske, William R. Yamamura: Dept. of Pharmacology, University of Arizona Health Sciences Center, Tucson, AZ 85724 **The influence of guanyl-5'-yl imidodiphosphate and sodium chloride on the binding of the muscarinic agonist, (3H)cis methyldioxolane.** European Journal of Pharmacology. 61(3):317-318, 1980.

Guanyl-5'-yl imidodiphosphate (Gpp(NH)p) reduced the binding of the muscarinic agonist (3H)cis methyldioxolane (3H-CD) to muscarinic cholinergic receptors in the rat forebrain and longitudinal muscle of the ileum by about 90%. Sodium chloride (NaCl) also produced a concentration dependent inhibition of 3H-CD binding in these tissues. Results indicate that Gpp(NH)p and NaCl reduce the affinity of superhigh and high affinity receptors or convert these higher affinity receptors into low affinity receptors. 5 references.

002749 Eikelboom, Roelof; Stewart, Jane. Dept. of Psychology, Concordia University, 1455 de Mainsonneuve Blvd., Montreal, Quebec, Canada, H3G 1M8 **Conditioned temperature effects using morphine as the unconditioned stimulus.** Psychopharmacology. 61(1):31-38, 1979.

The conditioning of body temperature changes using an injection of morphine sulphate as the conditioned stimulus was investigated in 30 male Wistar rats. During conditioning, animals in the morphine groups, when compared to the saline control animals, showed a conditioned anticipatory hypothermia in the preinjection environment that was opposite in direction to the unconditioned hyperthermia to morphine. In contrast, in the injection environment, animals in the morphine groups showed a conditioned hyperthermia when tested after the period abstinence. These results suggest a complex interaction between the conditioned and unconditioned temperature responses to morphine. 13 references. (Author abstract modified)

002750 Eikenburg, D. C.; Stickney, J. L. Stickney: Dept. of Pharmacology and Toxicology, Michigan State University, East Lansing, MI 48824 **Cardiac effects of 1-alpha-acetylmethadol. V. Possible involvement of the autonomic nervous system.** Toxicology and Applied Pharmacology. 51(1):91-100, 1979.

The cardiovascular responses of 1-alpha-acetylmethadol (LAAM) and its two major metabolites, 1-alpha-acetylnormethadol (N-LAAM) and 1-alpha-acetyldinormethadol (DN-LAAM), were examined in anesthetized dogs. LAAM, N-LAAM, and DN-LAAM caused significant decreases in mean arterial blood pressure (BP), heartrate (HR), and myocardial contractile force (CF). N-LAAM appeared to be approximately 10 times more potent than LAAM or DN-LAAM in producing these effects. The cardiovascular responses to LAAM were also studied in vagotomized (VAGOT), chemically sympathectomized (SYMX), and vagotomized and chemically sympathectomized (VAGOT SYMX) dogs. VAGOT had little effect on the response to LAAM. SYMX and VAGOT SYMX caused a decrease in the magnitude of the bradycardia produced by LAAM relative to that observed in intact animals and also increased the threshold dose required to produce significant decreases in BP; however, statistically significant decreases in BP, HR, and CF were observed. The data suggest that part of the hypotension and bradycardia produced by LAAM may be the result of sympathetic nervous system depression, but there also appears to be a direct component to the cardiovascular effects of LAAM and congeners. 25 references. (Author abstract)

002751 Eison, Michael Steven. University of California, Los Angeles **The regional distribution of amphetamine and its effects upon local glucose utilization in discrete areas of rat brain during continuous amphetamine administration. (Ph.D. dissertation).** Dissertation Abstracts International. 41(1):398-B, 1980. Ann Arbor, Univ. Microfilms No. 8015969, 150p., 1980.

The regional distribution of labeled materials following acute or continuous regimens of (3H)d-amphetamine administration and their effects upon local glucose utilization were investigated in the rat using liquid scintillation techniques. Amphetamine and its labeled derivatives were found to be selectively accumulated in certain brain regions, particularly in dopamine rich areas of the brain, and different regimens of amphetamine administration differentially affected local neural activity as reflected in glucose metabolism. Regional differences in glucose utilization as reflected in cumulative retention of counts 45 min after acute administration of (3h)2-deoxy-d-glucose were observed, and alterations in glucose utilization paralleled changes in amphetamine distribution for many of the regions studied. It is proposed that the selective activation of mesolimbic but not nigrostriatal or other brain mechanisms observed after 5 days of continuous amphetamine administration may, in this animal model, identify the dopamine involvement in the etiology of psychosis and schizophrenia. (Journal abstract modified)

002752 Erdmann, Erland; Krawietz, Wolfgang; Philipp, Gunther; Hackbarth, Ingelore; Schmitz, Wilhelm; Scholz, Hasso; Crane, Frederick L. Mediziniche Klinik I, Klinikum Grosshadern, Universitat Munchen, D-8000 Munich 70, Germany **Purified cardiac cell membranes with high (Na K)ATPase activity contain significant NADH-vanadate reductase activity.** Nature. 282(5736):335-336, 1979.

The mechanism of the claimed transient stimulatory action of high concentrations of vanadate on (Na K)ATPase activity of animals was investigated. Results indicate that there is a rapid loss of NADH in the ATPase assay, and that this loss is caused by an oxidation of NADH as a result of a NADH dependent reduction of vanadate. It is noted that the purified cardiac cell membranes used in the experiments contain high amounts of vanadate reductase activity. 17 references. (Author abstract modified)

002753 Eriksson, T.; Liljequist, S.; Carlsson, A. Dept. of Pharmacology, University of Goteborg, Fack S-400 33 Goteborg, Sweden **Ethanol-induced increase in the penetration of exoge-**

**nously administered L-dopa through the blood-brain barrier.** Journal of Pharmacy and Pharmacology. 31(9):636-637, 1979.

Whole brain levels of dopa and dopamine were determined in male Sprague-Dawley rats pretreated with ethanol (2mg/kg i.p.) or saline 20 minutes prior to injection of L-dopa (100mg/kg i.p.). Whole brain concentrations of dopa and dopamine were higher in animals pretreated with ethanol than in controls, and this difference persisted for at least 80 minutes. The ratio of brain dopa to plasma dopa was also significantly elevated in the ethanol treated rats 20, 40, and 80 minutes after the L-dopa injection. Subsequent studies showed that ethanol has a similar effect on the distribution of exogenous tyrosine, tryptophan, and alpha-methyldopa. These findings suggest that ethanol facilitates the penetration of the blood-brain barrier by dopa and other amino acids. 10 references.

**002754** Euvrard, Catherine; Boissier, Jacques R. Roussel-Uclaf, 111 route de Noisy, F-93230 Romainville, France **Biochemical assessment of the central 5-HT agonist activity of RU 24969 (a piperidinyl indole).** European Journal of Pharmacology. 63(1):65-72, 1980.

The piperidinyl indole derivative RU-24969 caused a dose dependent reduction in 5-hydroxyindoleacetic acid (5-HIAA) concentrations in male Sprague-Dawley rat forebrain and brainstem. This decrease in 5-HIAA appeared to be due to a decrease in serotonin (5-HT) turnover. Basal or 5-HT stimulated adenylate cyclase activities in colliculi from newborn rats were not affected by RU-24969. Serum prolactin and corticosterone levels were increased by RU-24969 in a dose dependent manner. Results suggest that RU-24969 is a potent 5-HT receptor agonist in rat brain. 25 references. (Author abstract modified)

**002755** Evans, R. H. Dept. of Pharmacology, Medical School, University Walk, Bristol BS8 1TD, England **Baclofen: lack of effect on neurotransmission in the mouse vas deferens.** Journal of Pharmacy and Pharmacology. 31(9):642-643, 1979.

The effects of baclofen on neurotransmission in the mouse vas deferens, frog spinal cord, and rat superior cervical ganglion were compared. A marked depressant action was seen in the frog spinal cord. In contrast, transmission in the superior cervical ganglion and vas deferens elicited by electrical field stimulation was not altered by baclofen in concentrations up to 1mM. These findings demonstrate the selective action of baclofen and do not support the suggestion that a beta-phenethylamine receptor is involved in the action of baclofen. 10 references.

**002756** Evans, R. H.; Francis, A. A.; Hunt, K.; Oakes, D. J.; Watkins, J. C. Dept. of Pharmacology, Medical School, University Walk, Bristol BS8 1TD, England **Antagonism of excitatory amino acid-induced responses and of synaptic excitation in the isolated spinal cord of the frog.** British Journal of Pharmacology. 67(4):591-603, 1979.

The structure/activity relations of monoamino and diamino dicarboxylic acids were studied in the isolated hemisected frog spinal cord. L-monoamino dicarboxylic acids of chain length up to eight carbon atoms were all agonists of excitatory amino-acid-induced responses. Within a series of D-monoamino dicarboxylic acids and diamino dicarboxylic acids, there was a progression from agonist activity for compounds of chain length equal or shorter than glutamate to antagonist activity for compounds of longer chain length. The antagonist actions of these substances showed a magnesium-like selectivity with respect to depolarizations produced by different excitants. N-methyl-D-aspartate (NMDA) was the most susceptible agonist. The relative potencies of the compounds as NMDA antagonists paralleled their relative potencies as depressants of synaptic responses. Results suggest there are different types of excitatory amino acid receptors and that NMDA and its antagonists act predominantly on one type. 39 references. (Author abstract modified)

**002757** Extein, Irl; Lo, Chi-man; Goodwin, Frederick K.; Schoenfeld, Ronald I. Fair Oaks Hospital, 19 Prospect St., Summit, NJ 07901 **Dopamine-mediated behavior produced by the enkephalin analogue FK 33-824.** Psychiatry Research. 1(3):333-339, 1979.

FK 33-824, an extremely potent analogue of met-enkephalin with a spectrum of action similar to the endogenous opiate-like peptides, was used to investigate the behavioral role of the endogenous opiate-like peptide systems. Intraperitoneal injection of FK 33-824 produced apomorphine-like stereotyped behavior in rats. Antagonism of this stereotype by naloxone and neuroleptics is reported. It is suggested that FK 33-824 can activate opiate and dopamine receptors in the brain. Results are discussed in terms of a possible mechanism for the reported improvement in schizophrenic psychosis produced by naloxone. 34 references. (Author abstract modified)

**002758** Farsang, Csaba; Kunos, George. Dept. of Pharmacology and Therapeutics, McGill University, Montreal, Quebec, Canada H3G 1Y6 **Naloxone reverses the antihypertensive effect of clonidine.** British Journal of Pharmacology. 67(2):161-164, 1979.

In unanesthetized, spontaneously hypertensive Okamoto-Aoki rats, the decrease in blood pressure and heartrate produced by clonidine (5 to 20mcg/kg i.v.) was inhibited or reversed by naloxone (0.2 to 2mg/kg i.p.). The hypotensive effect of alpha-methyldopa (100mg/kg i.p.) was also partially reversed by naloxone. Naloxone alone had no effect on blood pressure and heartrate. In brain membranes from spontaneously hypertensive rats, clonidine did not alter the stereoselective binding of tritiated naloxone and naloxone had no influence on the clonidine supressible binding of tritiated dihydroergocryptine. Results indicate that the effects of central alpha-adrenoceptor stimulation in spontaneously hypertensive rats involve activation of opiate receptors. The functional antagonism of naloxone and clonidine suggests that clonidine may cause the release of an endogenous opiate involved in central control of sympathetic tone. 20 references. (Author abstract modified)

**002759** Fehm, H. L.; Voigt, K. H.; Lang, R. E.; Pfeiffer, E. F. Abteilung Innere Medizin I, Zentrum fur Innere Medizin und Kinderheilkunde, Universitat Ulm, Steinhovelstr. 9, D-7900 Ulm, Germany **Effects of neurotransmitters on the release of corticotropin releasing hormone (CRH) by rat hypothalamic tissue in vitro.** Experimental Brain Research. 39(2):229-234, 1980.

Effects of neurotransmitters on in vitro release of corticotropin releasing hormone (CRH) from rat hypothalamic tissue were investigated. Norepinephrine (NE) at a concentration of less than two times 10 to the -6 M stimulated dose related CRH release but the response decreased at larger concentrations. The action of NE was completely blocked by coincubation with phentolamine. These results suggest that in the rat, NE may have a physiological role as stimulator of CRH release at the level of the mediobasal hypothalamus. However, in view of the conflicting results obtained with similar and other methods, no definite conclusions should yet be drawn. 38 references. (Author abstract modified)

**002760** Fennessy, M. R.; Laska, F. J. Dept. of Pharmacology, University of Melbourne, Parkville, Victoria, 3052 Australia **Acute effects of opiate agonists, partial agonists and antagonists on brain monoamines in the rat.** Archives Internationales de Pharmacodynamie et de Therapie. 238(1):60-70, 1979.



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The effects of single doses (4.5mg/kg i.p.) of morphine, cyclazocine, pentazocine, levallorphan, nalorphine, naloxone, naltrexone, and dextrophan on behavior and biogenic amine metabolism in female Wistar rats were examined. Only morphine and cyclazocine altered behavior. The serotonin metabolite 5-hydroxyindoleacetic acid was the only substance consistently elevated by all the compounds tested. Results suggest that a causal relationship between the acute effects of opiate agonists, partial agonists, and antagonists on brain serotonin metabolism and their pharmacological actions is unlikely. 39 references. (Author abstract modified)

**002761** Feuerstein, Giora; Govrin, Hanna; Kapitulnik, Jaime. Kapitulnik: Dept. of Pharmacology, Hebrew University-Hadassah Medical School, Jerusalem, Israel **Lithium-induced increase in the metabolism of benzo(a)pyrene and drugs in rat liver.** Biochemical Pharmacology. 28(21):3167-3170, 1979.

Administration of lithium chloride (2.5mEq/kg/day) to rats for 4 or 12 days increased the rates of hepatic hydroxylation of benzo(a)pyrene, antipyrine, and zoxazolamine by 100%, 114%, and 56%, respectively, and the rate of hepatic conjugation of 4-methylumbelliferone with glucuronic acid by 19%. Liver lithium levels were highly correlated with plasma lithium levels but not with hepatic benzo(a)pyrene hydroxylase activities. In vitro addition of lithium to liver 10,000 g supernatants did not affect the hydroxylation of benzo(a)pyrene, suggesting that the lithium-induced increase in hepatic drug hydroxylation is not due to enzyme activation and is probably a result of lithium mediated enzyme induction. 16 references. (Author abstract)

**002762** Fonlupt, P.; Roche, M.; Cronenberger, L.; Pacheco, H. Service de Chimie Biologique, Institut National des Sciences Appliquees, 20 Avenue Albert Einstein, F-69621 Villeurbanne, Cedex, France **Action of S-adenosyl-L-homocysteine on the metabolism of dopamine, norepinephrine and serotonin in rat brain.** Archives Internationales de Pharmacodynamie et de Therapie. 240(1):35-44, 1979.

S-adenosylhomocysteine (SAH, 0.1 to 30mg/kg i.p.) increased the synthesis of tritiated norepinephrine from tritiated tyrosine in male Wistar rat brainstem and midbrain, but did not alter tissue catecholamine levels. SAH decreased serotonin synthesis and tissue levels and increased 5-hydroxyindoleacetic acid levels. No changes in dopamine metabolism were observed. The effect of SAH on amine metabolism began 1 hour after drug administration and persisted 6 hours later, which is consistent with the time course of the hypnotic effect of SAH. 24 references. (Author abstract modified)

**002763** Fratta, Walter; Casu, Mariano; Balestrieri, Angelo; Loviselli, Andrea; Biggio, Giovanni; Gessa, Gian Luigi. Institute of Pharmacology, University of Cagliari, Cagliari, Italy **Failure of ketamine to interact with opiate receptors.** European Journal of Pharmacology. 61(4):389-391, 1980.

Ketamine did not displace 3H-dihydromorphine or 3H-methionine-enkephalin from opiate receptors in male Sprague-Dawley rat brain synaptosomal mitochondrial membrane preparations. Naloxone did not antagonize analgesia induced by ketamine in rats. Results suggest that ketamine analgesia is not mediated by opiate receptors, even though the drug has several morphine life effects. 9 references. (Author abstract modified)

**002764** Fujita, Norihisa; Saito, Kihachi; Iwatsubo, Katsuya; Hirata, Akira; Noguchi, Yutaka; Yoshida, Hiroshi. Dept. of Pharmacology I, Osaka University School of Medicine, Nakanoshima 4-3-57, Kitaku, Osaka 530, Japan **Binding of (3H)apomorphine to striatal membranes prepared from rat brain after 6-hydroxydopamine and kainic acid lesions.** Brain Research. 190(2):593-596, 1980.

The binding of (3H)apomorphine to striatal membranes from male Sprague-Dawley rats after 6-hydroxydopamine (6-OHDA) and kainic acid lesions was examined. The specific binding of (3H)apomorphine to striatal membranes prepared from 6-OHDA lesioned rats was saturable biphasically. It was further observed that unilateral injection of 6-OHDA followed by kainic acid lesions with a 3 week interval diminished the specific (3H)apomorphine binding to striatal membranes. The results demonstrate biphasic (3H)apomorphine binding in the crude synaptic membrane fraction prepared from rat brain. 9 references.

**002765** Fukumori, Ryuji; Minegishi, Akemi; Satoh, Tetsuo; Kitagawa, Haruo; Yanaura, Saizo. Satoh: Dept. of Drug Evaluation and Toxicological Sciences, Faculty of Pharmaceutical Sciences, Chiba University, Chiba, Japan **Changes in the serotonin and 5-hydroxyindoleacetic acid contents in rat brain after ethanol and disulfiram treatments.** European Journal of Pharmacology. 61(2):199-202, 1980.

Disulfiram (700mg/kg, orally) significantly increased brain levels of serotonin (5-HT) and 5-hydroxyindoleacetic acid (5-HIAA) in male Wistar rats. Ethanol (one 1g/kg i.p. injection or two 1.5g/kg injections) did not alter the 5-HT level, but the higher dose significantly increased 5-HIAA. Brain 5-HT was significantly increased and 5-HIAA was significantly reduced in rats treated with disulfiram in combination with ethanol, compared to those treated with disulfiram alone. Results suggest that the biogenic aldehyde derived from 5-HT, may influence 5-HT metabolism and the elimination of 5-HIAA from the brain. 10 references. (Author abstract modified)

**002766** Fuller, R. W.; Perry, K. W.; Snoddy, H. D. Lilly Research Laboratories, Eli Lilly and Co., Indianapolis, IN 46206 **In vivo effects of LR5182, cis-3-(3,4-dichlorophenyl)-2-N, N-dimethylaminomethyl-bicyclo-(2,2,2)-octane hydrochloride, an inhibitor of uptake into dopamine and norepinephrine neurons.** Neuropharmacology. 18(5):497-501, 1979.

In male Cox mice, cis-3-(3,4-dichlorophenyl)-2-N, N-dimethylaminomethyl-bicyclo-(2,2,2)-octane hydrochloride (LR5182) antagonized the depletion of heart norepinephrine by 6-hydroxydopamine, but did not alter the depletion of brain serotonin by p-chloramphetamine. In male Wistar rats, LR5182 antagonized the depletion of norepinephrine in the cerebral hemispheres and in the hypothalamus after injection of alpha-methyl-m-tyrosine (aMMT); the drug also antagonized dopamine depletion in the cerebral hemispheres, but not epinephrine depletion in the hypothalamus of these rats. The concentration of alpha-methyl-m-tyramine and of metaraminol in the cerebral hemispheres of rats was lowered by LR5182 after aMMT injection, suggesting the inhibition of uptake into dopamine and norepinephrine neurons. LR5182 significantly enhanced the elevation of brain 3,4-dihydroxyphenylacetic acid concentration by spiperone in rats. 15 references. (Author abstract modified)

**002767** Fulton, A.; Burrows, G. D. Dept. of Psychiatry, Melbourne University, Victoria, Australia **3H-haloperidol binding to tissue receptors: influence of some drugs and antipsychotic potency.** Life Sciences. 26(18):1505-1508, 1980.

The drug concentrations which inhibited 50% of 3H-haloperidol specific binding (the IC50) by striatal receptors of fluphenazine dihydrochloride, 7-hydroxy fluphenazine, chlorpromazine hydrochloride, 7-hydroxy chlorpromazine, pericyazine, and nomifensine were measured, and were found to be 2.7nM, 3.3nM, 6.3nM, 4.7nM, 360mM respectively. Fluphenazine sulphoxide and the glucuronide of 7-hydroxy chlorpromazine were inactive in competing for binding sites in the rat corpus striata. It is noted that the IC50 of fluphenazine dihydrochloride, chlorpro-

mazine, and pericyazine followed in the same ranking order as their daily clinical doses as antipsychotics. 11 references. (Author abstract)

**002768** Furlow, T. W., Jr.; Hallenback, J. M.; Goodman, J. C. Dept. of Neurology, University of Alabama, Birmingham, AL 35294 **Adrenergic blocking agents modify the auditory-evoked response in the rat.** Brain Research. 189(1):269-273, 1980.

The audioevoked response (AER) in male Sprague-Dawley rats was altered in distinctive and contrasting ways by phentolamine and propranolol. These alterations in the AER parallel opposing changes in local glucose utilization induced by the alpha-adrenergic and beta-adrenergic blocking agents in the auditory pathways of the rat. Results suggest that a reciprocal adrenergic mechanism consisting of inhibitory alpha-receptors and facilitatory beta-receptors may modulate brainstem auditory function. 24 references.

**002769** Gahwiler, B. H.; Dreifuss, J. J. Pharmaceutical Division, Preclinical Research, Sandoz, Ltd., Basel, Switzerland **Transition from random to phasic firing induced in neurons cultured from the hypothalamic supraoptic area.** Brain Research. 193(2):415-425, 1980.

Intracellular recording was used to study the effects of drugs that cause vasopressin release on the activity of cultured neurons from the rat hypothalamic preoptic area. Nicotine and acetylcholine caused a transition from random to a phasic discharge pattern. Enkephalin analogues induced similar alterations, which were blocked by naloxone. Glutamate caused a dose dependent excitation of the hypothalamic neurons, but did not induce phasic firing. Angiotensin-II increased the firing rate in randomly firing cells and the duration of bursts in phasic cells. 51 references. (Author abstract modified)

**002770** Gal, E. Martin; Sherman, Arnold D. Neurochemical Research Laboratories, College of Medicine, University of Iowa, Iowa City, IA 52242 **L-Kynurenine: its synthesis and possible regulatory function in brain.** Neurochemical Research. 5(3):223-239, 1980.

Interrelationships between the L-kynurenine and 5-hydroxyindole pathways and some aspects of the properties and function of the cerebral indolamine-2,3-dioxygenase are discussed. Cerebral levels and synthesis of kynurenine; cerebral uptake and utilization of L-tryptophan and L-kynurenine; cerebral metabolism of kynurenines, 5-HT, 5-HIAA, and tryptophan loading; hydroxylation of tryptophan and its relation to hydroxylated kynurenines; and the effect of kynurenine loading are considered. Enzymes participating in synthesis of kynurenines as determined by in vitro studies are examined. Suggestions are made for further research. 44 references.

**002771** Gallager, Dorothy W.; Mallorga, Pierre; Tallman, John F. Section on Biochemistry and Pharmacology, Biological Psychiatry Branch, NIMH, Bethesda, MD 20205 **Interaction of diphenylhydantoin and benzodiazepines in the CNS.** Brain Research. 189(1):209-220, 1980.

The anticonvulsant diphenylhydantoin enhanced the ability of diazepam to inhibit neuronal firing in the dorsal raphe nucleus of Sprague-Dawley rats. This was associated with enhanced specific binding of (3H)diazepam due to an increased number of benzodiazepine binding sites. The effects of diphenylhydantoin on benzodiazepine binding were independent of GABA. It is suggested that the benzodiazepine binding site is involved in convulsant and anticonvulsant activity. 44 references. (Author abstract modified)

**002772** Gamse, R.; Holzer, P.; Lembeck, F. Lembeck: Institut fur Experimentelle und Klinische Pharmakologie, Universitat Graz, Universitatsplatz 4, A-8010 Graz, Austria **Indirect evidence for presynaptic location of opiate receptors on chemosensitive primary sensory neurones.** Naunyn-Schmiedeberg's Archives of Pharmacology. 308(3):281-285, 1979.

The binding of tritiated diprenorphine was examined in homogenates of whole spinal cord or upper dorsal horn from 5-month-old rats that had been pretreated subcutaneously with 50mg/kg capsaicin or solvent on the second day of life. The capsaicin pretreatment resulted in a 17% decrease of opiate binding sites in the whole spinal cord and a 37% decrease in the upper dorsal horn, with no change in binding affinity. The degeneration of chemosensitive primary sensory neurons induced by capsaicin suggests that some opiate receptors are located presynaptically on the central terminals of these neurons. 22 references. (Author abstract modified)

**002773** Garrigou, Danielle; Blozovski, Denise. Laboratoire de Psychophysiologie, Universite Pierre et Marie Curie, Paris, France **Parachlorophenylalanine and atropine influences on theta activity in the young rat.** Behavioral and Neural Biology. 29(3):365-371, 1980.

The effects of parachlorophenylalanine (pCPA) and atropine on theta activity in the young rat were examined. pCPA increased the probability of occurrence of alert immobility and related atropine sensitive rhythmic slow activity (RSA) during free behavior and passive avoidance conditioning in chronic 17-day-old rats. Nonlocomotor activity was diminished and frequencies of movement related RSA were slightly decreased. Atropine, which completely abolished pCPA-induced alert immobility and related slow RSA, highly alerted fast RSA, reducing its incidence and increasing its frequencies. The amplitude, frequency, and regularity of movement related RSA varied with the state of alertness during conditioning in normal and pCPA treated rats. The results suggest that RSA production depends largely on central muscarinic mechanisms with serotonergic components having a modulatory effect, and support the hypothesis that RSA in the rat is not only correlated with voluntary movement but is also dependent on the alert state. 10 references. (Author abstract)

**002774** Gentleman, S; Parenti, M.; Commissiong, J. W.; Neff, N. H. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Dopamine-activated adenylate cyclase of spinal cord: supersensitivity following transection of the cord. (Unpublished paper).** Washington, DC, NIMH, 1979. 17 p.

A dopamine (DA) activated adenylate cyclase has been identified in a membrane fraction of rat spinal cord: the concentration of DA producing half maximal activation is about 5mcM and the activation is blocked by haloperidol. Apomorphine also activates the cyclase. In the presence of guanosine triphosphate (GTP) and sucrose and cord membrane, fraction can be frozen for several days without loss of DA activated cyclase. Following transection of cord, adenylate cyclase becomes about five to 10 times more sensitive to DA below the transection. The presence of DA activated adenylate cyclase in the cord is consistent with reports of dopamine tracts in spinal cord. This neuronal system may play an essential role in normal spinal mechanisms, in disease associated with dopaminergic neurons, as well as in the side-effects of neuroleptic drugs. 15 references. (Author abstract)

**002775** Gershon, M. D.; Jonakait, G. Miller. Dept. of Anatomy, Columbia University, College of Physicians and Surgeons, New York, NY 10032 **Uptake and release of 5-hydroxytrypta-**

**mine by enteric 5-hydroxytryptaminergic neurones: effects of fluoxetine (Lilly 110140) and chlorimipramine.** British Journal of Pharmacology. 66(1):7-9, 1979.

The effects of fluoxetine on the uptake of 5-hydroxytryptamine (5-HT) by enteric neurons were examined and the effects of fluoxtetine and chlorimipramine (CMI) on the efflux of tritiated 5-HT from the myenteric plexus were compared. Fluoxetine was a competitive inhibitor of 5-HT uptake by the guinea-pig myenteric plexus and was a more potent uptake inhibitor than CMI. However, the enhanced efflux of (3H)5-HT seen after CMI suggested that CMI not only inhibited uptake but also released 5-HT. These findings are similar to those reported in central 5-HT neurons and indicate that enteric 5-HT neurons are a useful model for studying the central serotonergic effects of drugs. 10 references. (Author abstract modified)

**002776** Gibbs, Daniel Marion. Emory University **The role of dopamine in the regulation of prolactin secretion. (Ph.D. dissertation).** Dissertation Abstracts International. 40(1):100-B, 1979. Ann Arbor, Univ Microfilms No. 7912742, 112p., 1978.

Experiments designed to test the hypothesis that dopamine is a prolactin inhibiting factor are reported. A technique was developed for collection of pituitary stalk blood in the rat and dopamine concentration was measured. The effects of histamine and acetylcholine on plasma prolactin concentrations were investigated. Whether the amount of dopamine in stalk plasma was sufficient to inhibit prolactin secretion and whether changes in prolactin secretion could be accounted for by small changes in dopamine secretion were also studied. The results of these experiments establish dopamine as a physiologic, tonic prolactin inhibiting factor, but they strongly suggest that the hypothalamic regulation of prolactin secretion involves other factors as well. (Journal abstract modified)

**002777** Giesing, Michael; Zilliken, Friedrich. Institute for Physiological Chemistry, Rheinische Friedrich-Wilhelms Universitat Bonn, Nussallee 11, D-5300 Bonn, Germany **Lipid metabolism of developing central nervous tissues in organotypic cultures. III. Ganglionic control of glycerolipids and fatty acids in cortex grey matter.** Neurochemical Research. 5(3):257-270, 1980.

Lipid changes in rat brain grey matter were observed in a coculture system of innervating and target explants. The de novo biosynthesis of individual glycerolipids and the metabolism of fatty acids were investigated. Innervating grey matter cultures exhibited a substantial increase in neutral glycerolipid formation. Only slight modifications were observed in the fatty acid fraction. Target cells responded to innervation by a marked increase in phosphatidylcholine, phosphatidylinositol, and phosphatidylethanolamine formation. In addition, the biosynthesis of arachidonate and docosahexaenoate was drastically enhanced. It is shown that neuritic bridges connecting the explants, rather than soluble factors, account for the effects observed. Putative mechanisms involved in changes of lipid metabolism are discussed. 40 references. (Author abstract)

**002778** Gimeno, M. F.; Landa, A.; Sterin-Speziale, N.; Cardinali, D. P.; Gimeno, A. L. Gimeno, A. L.: Centro de Estudios Farmacologicos y de Principios Naturales, V. de Obligado 2490, 1428 Buenos Aires, Argentina **Melatonin blocks in vitro generation of prostaglandin by the uterus and hypothalamus.** European Journal of Pharmacology. 62(4):309-317, 1980.

The effects of melatonin on prostaglandin (PG) release from uterine horns of spayed Wistar rats and from bovine medial basal hypothalamic explants were examined. The output of PGE and PGF-like material from both preparations was diminished by melatonin. Similarities between the effects of melatonin and indomethacin are discussed. 31 references. (Author abstract modified)

**002779** Giraud, Pierre; Lissitzky, Jean-Claude; Conte-Devolx, Bernard; Gillioz, Pierre; Oliver, Charles. Laboratoire de Medecine Experimentale, UER de Medecine Nord, Blvd. Pierre Dramard, F-13326 Marseille Cedex 03, France **Influence of haloperidol on ACTH and beta-endorphin secretion in the rat.** European Journal of Pharmacology. 62(2/3):215-217, 1980.

The dopamine receptor blocker haloperidol (1mg/kg i.p.) induced a large increase in plasma ACTH and beta-endorphin-like immunoreactivity in male Sprague-Dawley rats. This effect was blocked by pretreatment with corticosteroids. Results suggest that catecholamines inhibit ACTH and beta-endorphin secretion in the rat. 11 references. (Author abstract modified)

**002780** Glossmann, Hartmut; Hornung, Rainer. Rudolf Buchheim Institut fur Pharmakologie, Frankfurter Strasse 107, D-6300 Giessen, Germany **Alpha-adrenoceptors in rat brain: sodium changes in the affinity of agonists for prazosin sites.** European Journal of Pharmacology. 61(4):407-408, 1980.

The effects of sodium on the binding of agonists to rat brain alpha-adrenoceptors labeled with 3H-prazosin were examined. The interaction of prazosin with its receptor was not altered by the inclusion of 150mM sodium chloride, but a sodium shift was observed for all agonists tested. This shift in affinity differed in direction and in extent for different agonists: (-)-adrenaline, (-)-noradrenaline, and alpha-methylnoradrenaline showed a decrease in affinity, while (-)-phenylephrine, clonidine, and naphazoline increased their affinity for prazosin sites. The rank order of potency for these agonists was also altered by sodium. 5 references.

**002781** Gordon, John H.; Borison, Richard L.; Diamond, Bruce I. Dept. of Pharmacology, Chicago Medical School, 2020 West Ogden Avenue, Chicago, IL 60612 **Modulation of dopamine receptor sensitivity by estrogen.** Biologial Psychiatry. 15(3):389-396, 1980.

The effects of estrogen in an animal model of tardive dyskinesia were investigated. Ovariectomized rats were treated daily for 16 days with haloperidol or Haldol plus estradiol benzoate (EB). Rats were then challenged with d-amphetamine or apomorphine 1 week following cessation of the chronic treatments. Chronic treatments with eitherr Haldol or EB alone produced an enhanced response to both d-amphetamine and apomorphine, while the combined treatment produced a synergistic response. Rats treated chronically with Haldol, and treated daily with EB following the Haldol treatment, showed an attenuation of drug-induced stereotypy. It is concluded that these preliminary data indicate that estrogen can attentuate the development or mask the display of the supersensitive dopamine receptor. 27 references. (Author abstract modified)

**002782** Gothert, M.; Weinheimer, G. Pharmakologisches Institut der Universitat Essen, Hufelandstrasse 55, D-4300 Essen 1, Germany **Extracellular 5-hydroxytryptamine inhibits 5-hydroxytryptamine release from rat brain cortex slices.** Naunyn-Schmiedeberg's Archives of Pharmacology. 310(1):93-96, 1979.

The effects of extracellular 5-hydroxytryptamine (5-HT) on the release of 5-HT from serotonergic neurons of male Wistar rat brain cortex slices were examined. The slices were preincubated with tritiated 5-HT and then superfused with physiological salt solution and stimulated electrically or superfused with calcium (Ca2) free solution containing 25mM potassium and stimulated by addition of 1.3mM calcium chloride. After blockade of neuronal 5-HT uptake with clomipramine or paroxetine, the tritium overflow evoked by both methods of stimulation was

decreased by unlabeled 5-HT and increased by methiothepin. The inhibition caused by 5-HT was antagonized by simultaneous administration of methiothepin. The inhibition by 5-HT of Ca2-induced overflow was also observed in the presence of tetrodotoxin. Results suggest that 5-HT regulates its own release from central serotonergic neurons by activating presynaptic autoreceptors, thereby decreasing the availability of Ca2 for stimulus/release coupling. 16 references. (Author abstract modified)

**002783** Grandison, Lindsey; Fratta, Walter; Guidotti, Alessandro. Dept. of Physiology and Biophysics, Rutgers Medical School, CMDNJ, Piscataway, NJ 08854 **Location and characterization of opiate receptors regulating pituitary secretion.** Life Sciences. 26(19):1633-1642, 1980.

The site at which opiate agonists and antagonists act to alter secretion of prolactin, growth hormone, and luteinizing hormone as well as the pharmacological specificity of the opiate receptors mediating these effects were examined in rats. Injection of beta-endorphin but not a tenfold higher dose of the nonopiate peptide beta-endorphin, increased release of prolactin and growth hormone in male rats while inhibiting luteinizing hormone release in ovariectomized estrogen primed female rats. Prior treatment with naltrexone blocked these responses. Injection of naltrexone into the hypothalamus lowered prolactin release. In rats with a surgically formed hypothalamic island systemic administration of morphine or naltrexone altered prolactin release in the same manner as was observed in intact animals. In contrast, no effects of beta-endorphin or naltrexone were observed on the spontaneous secretion of prolactin in vitro. In addition beta-endorphin did not alter the inhibition of prolactin release produced by apomorphine in vitro. The ED50 for stimulation of prolactin release following intraventricular administration of beta-endorphin or the synthetic enkephalin analog FK 33-824 was the same, approximately 0.1ng/rat. However FK 33-824 at 0.2ng/rat was able to produce much greater analgesia and catatonia than beta-endorphin. The metabolism and distribution of beta-endorphin was examined but did not account for these differential effects. These results indicate that opiate agonists and antagonists can act at the hypothalamic but not the anterior pituitary level to alter release of prolactin, growth hormone, and luteinizing hormone. In addition, the data suggest that the opiate receptors mediating release of prolactin may have a different pharmacological specificity from those involved with analgesia and catatonia. 24 references. (Author abstract)

**002784** Grecksch, Gisela; Ott, Tilmann; Matthies, Hansjurgen. Institute of Pharmacology and Toxicology, Medical Academy, 301 Magdeburg, Germany **The effect of intrahippocampally applied anisomycin on the retention of brightness discrimination in rats.** Behavioral and Neural Biology. 29(3):281-288, 1980.

The role of hippocampal protein synthesis in the consolidation of brightness discrimination in the rat was examined. Intrahippocampal application of the protein synthesis inhibitor anisomycin impaired the retention performance of a brightness discrimination task. A proactive effect of anisomycin could be excluded. The impairment of retention was not due to disturbing effects on locomotor activity. The same dosage of anisomycin caused a reduction in leucine incorporation into hippocampal proteins to approximately 6% to 9%. The present findings suggest that consolidation processes acting during and for a few hours after training may be impaired by inhibition of protein synthesis in the hippocampus. 32 references. (Author abstract)

**002785** Griauzde, Mindaugas L.; Chen, Edwin H.; Radulovacki, Miodrag. Radulovacki: University of Illinois at the Medical Center, P.O. Box 6998, Chicago, IL 60680 **Effects of diazepam on sleep, temperature, 5-hydroxyindoleacetic and homovanillic acids in cisternal cerebrospinal fluid of cats.** Pharmacology. 19(3):149-155, 1979.

The effects of diazepam (DZ) (0.3 to 1.5mg/kg, i.p.) on sleep, cisternal cerebrospinal fluid (CSF) concentrations of 5-hydroxyindoleacetic acid (5-HIAA) and homovanillic acid (HVA), and rectal temperature of cats were examined. The results show that administration of DZ produced a significant increase in slow-wave sleep (SWS) with a peak occurring at a dose of 0.9mg/kg. Futher increase in doses of DZ decreased SWS. DZ administration produced no change in paradoxical sleep, rectal temperature, 5-HIAA or HVA CSF levels. Lack of correlation between various doses of DZ, and 5-HIAA or HVA concentrations in the presence of an increased percentage of SWS suggests a possible mode of DZ action mediated through a mechanism independent of monoamines. It is concluded that usually monoamines are associated with normal sleep. 36 references. (Author abstract modified)

**002786** Grol, Cor J.; Rollema, Hans; Asselbergs, Hans W. Rollema: Laboratory for Pharmaceutical and Analytical Chemistry, Antonius Deusinglaan 2, State University, Groningen, The Netherlands **The effect of 2-substitution on conformations and brain concentrations of phenothiazine-neuroleptics in relation to dopamine-antagonism.** Journal of Pharmacy and Pharmacology. 31(10):667-671, 1979.

Conformational changes in phenothiazine neuroleptics (promazine, chlorpromazine, and triflupromazine) were studied in relation to dopamine antagonistic potency in rats. Results showed that the phenothiazines are flexible molecules and that many conformations exist in which either the sulfur atom or the 2-substituent can interact with dopamine receptor sites. The enhancing effect of 2-substitution on neuroleptic activity may be due to the increased probability of conformations in which the side chain is directed toward one side of the molecule and to a direct interaction with the receptor at a site corresponding with one of the dopamine oxygens. 17 references. (Author abstract modified)

**002787** Gross, Gerhard; Brodde, Otto-Erich; Schumann, Hans-Joachim. Institute of Pharmacology, University of Essen, D-4300 Essen, Germany **Decreased number of beta-adrenoceptors in cerebral cortex of hypothyroid rats.** European Journal of Pharmacology. 61(2):191-194, 1980.

The 3H-dihydroalprenolol binding assay was used to study the effect of thyroid hormone deficiency on beta-adrenoceptors in the male Wistar rat cerebral cortex. The density of beta-adrenoceptors was reduced by 37% in rats made hypothyroid by 6-propyl-2-thiouracil. Receptor affinity did not differ significantly in hypothyroid and euthyroid rats. 11 references. (Author abstract modified)

**002788** Grossfeld, Robert M. University of Texas at Austin, Austin, TX 78712 **Localization of glutamic-acid decarboxylase in nerves. (Unpublished paper).** Final Report, NIMH Grant R03-MH-32075, 1980. 8p.

The cellular localization of the enzyme glutamic acid decarboxylase (GAD) in crustacean peripheral nerves was studied as part of the broader study of the importance of biochemical exchanges between glia and nerve cell axons for long-term maintenance of neuronal function. The specific questions examined were: 1) are the 1976 results of Sarne, Schrier, and Gainer reproducible with isolated crayfish and lobster peripheral nerves and motor axons; 2) can GAD activity be measure accuratedly in axoplasmic and axolemma-glial sheath fractions prepared from isolated lobster motor axons; 3) do the axoplasmic and axolemma-glial sheath fractions of GAD, prepared by extrusion of lobster motor axons, truely originate from these two distinguish-

able cellular compartments; and 4) does the localization of GAD activity in either axoplasmic or axolemma-glial sheath fractions, prepared from lobster axons, merely reflect glial phagocytosis of degenerating axonal material in vitro. The results suggest that not only the axoplasm but also the axolemma-glial sheath may possess on e or more GABA-forming enzymes. The data also suggest that there may be a different cellular distribution of the GABA-forming and C02-forming enzyme activities.

**002789** Groves, Philip M.; Staunton, David A.; Wilson, Charles J.; Young, Stephen J. Dept. of Psychology, Muenzinger Building, Box 345, University of Colorado, Boulder, CO 80309 **Sites of action of amphetamine intrinsic to catecholaminergic nuclei: catecholaminergic presynaptic dendrites and axons.** Progress in Neuro-Psychopharmacology. 3(4):315-335, 1979.

Recent evidence is reviewed to support the suggestion that amphetamine acts at sites intrinsic to catecholaminergic nuclei by facilitating release of catecholamines from presynaptic dendrites, axon terminals, and possibly other regions of catecholaminergic nerve cells intrinsic to these cell groups. Evidence for the control of dopaminergic neurons through dendro-dendritic interactions, the functional localization of dopamine in the pars compacta of the substantia nigra, and dendritic release of dopamine in the substantia nigra is reviewed. Neurophysiological evidence for a functional role of dopamine in the substantia nigra in the control of dopaminergic activity is considered in relation to the action of amphetamine, and the sites of amphetamine intrinsic to the locus coeruleus are described. 75 references. (Author abstract modified)

**002790** Guaza, Carmen; Torrellas, Angeles; Borrell, Sara; Borrell, Jose. J. Borrell: Inst. de Endocrinologia y Metabolismo G. Maranon, Centro de Investigaciones Biologicas, Velazquez, 144, Madrid 6, Spain **The effects of acute and chronic administration of morphine on the turnover of brain and adrenal catecholamines in rats.** Psychopharmacology. 68(1):43-49, 1980.

Brain and adrenal catecholamine turnover was studied in female Wistar rats treated with morphine. In normal rats, catecholamine turnover was much slower in the adrenal glands than in the brain. Acute morphine treatment increased the turnover of brain and adrenal catecholamine, but chronic morphine treatment decreased the turnover of brain noradrenaline. Nalorphine-induced withdrawal resulted in increased utilization of brain noradrenaline and adrenal catecholamines. Results suggest that catecholamines may be involved in the mechanism of morphine tolerance and dependence. 41 references. (Author abstract modified)

**002791** Guidotti, A.; Baraldi, M.; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **1,4-Benzodiazepines and gamma-aminobutyric acid: pharmacological and biochemical correlates.** Pharmacology. 19(5):267-277, 1979.

The interaction of 1,4-benzodiazepines and GABA receptors was examined in a series of experiments using the NB2a subclone of mouse neuroblastoma and the C6 subclone of rat glioma cells. Results showed that the high affinity binding sites for 1,4-benzodiazepines and for GABA modulin were associated with GABA receptors in these two clones and that the reciprocal interactions between benzodiazepines and GABA observed in brain homogenates also occur in membranes of neuroblastoma and glioma cells. High affinity clonazepam binding to neuronal and glial cells was observed, but clonazepam failed to displace diazepam from its binding sites. The failure of clonazepam to displace diazepam binding was related to the lipid characteristics of the membranes and not to the properties of the receptor protein. 29 references. (Author abstract modified)

**002792** Gumulka, S. W.; Dinnendahl, V.; Schonhofer, P. S. Zentrum Pharmakologie und Toxikologie, Medizinische Hochschule Hannover, Postfach 61 01 80, D-3000 Hannover 61, Germany **Baclofen and cerebellar cyclic GMP levels in mice.** Pharmacology. 19(2):75-81, 1979.

Baclofen (3.5 to 10.0mg/kg) produced a dose dependent decrease in cerebellar cyclic guanosine monophosphate (GMP) content associated with a reduction in locomotor activity in male NMRI mice. Pretreatment with baclofen antagonized the rise in cerebellar cyclic GMP content induced by isoniazid and picrotoxin, but did not affect the increase in cyclic GMP following pentetrazole administration. Baclofen had little effect on arecoline-induced changes in cerebellar cyclic GMP content. Results indicate that baclofen exerts GABA agonistic activity at presynaptic sites. 26 references. (Author abstract modified)

**002793** Guyenet, Patrice G. Dept. of Pharmacology, University of Virginia School of Medicine, 1300 Jefferson Park Ave., Charlottesville, VA 22908 **The coeruleospinal noradrenergic neurons: anatomical and electrophysiological studies in the rat.** Brain Research. 189(1):121-133, 1980.

The neuroanatomical location and pharmacological sensitivity of coeruleospinal neurons were studied in male Sprague-Dawley rats. Coeruleospinal neurons were mulitipolar, medium sized cells and were found in the ventral division of the locus coeruleus and in the locus subcoeruleus. The firing rate of coeruleospinal cells identified by antidromic stimulation was slow and regular, with a conduction velocity characteristic of unmyelinated fibers. An anteriorly directed collateral was located in the midbrain reticular formation outside the main noradrenergic bundle. The coeruleospinal neurons were strongly inhibited by iontophoretic application of morphine, noradrenaline, clonidine, GABA and were excited by acetylcholine. 46 references. (Author abstract modified)

**002794** Haas, Helmut L.; Wieser, Heinz G. Neurochirurgische Klinik, Universitatsspital Zurich, CH-8091 Zurich, Switzerland **Effect of L-cycloserine on cortical neurons in the rat.** European Journal of Pharmacology. 61(1):79-83,1980.

The interaction of L-cycloserine and GABA was studied in rats. When administered by microionophoresis or i.p. injection, L-cycloserine depressed firing of neurons in the sensorimotor cortex, but did not modify the effects of endogenous or exogenous GABA. D-cycloserine had no effect on firing rate. It is concluded that L-cycloserine depresses cell firing by elevating GABA levels rather than by potentiating the action of GABA. 10 references. (Author abstract modified)

**002795** Haidamous, Madona; Kouyoumdjian, Jean C.; Briley, Patricia A.; Gonnard, Pierre. Gonnard: Departement de Biochimie, C.H.U. Henri-Mondor, Universite Paris XII, F-94010 Creteil Cedex, France **In vivo effects of noradrenaline and noradrenergic receptor agonists and antagonists on rat cerebellar cyclic GMP levels.** European Journal of Pharmacology. 63(4):287-294, 1980.

Noradrenaline and the postsynaptic alpha-adrenoceptor agonists methoxamine and phenylephrine increased cyclic guanosine monophosphate (cGMP) levels in the male Sprague-Dawley rat cerebellum. The alpha-adrenoceptor antagonists phentolamine and phenoxybenzamine decreased cGMP levels, but the presynaptic alpha-adrenoceptor antagonists yohimbine and piperoxane had no effect. Clonidine decreased cGMP levels at low doses, probably by inhibiting noradrenaline release, and this effect was antagonized by piperoxane or 6-hydroxydopamine pretreatment. The beta-noradrenergic agonist isoproterenol had no effect on cGMP levels, but the beta-noradrenergic antagonist propranolol

decreased cGMP levels. 46 references. (Author abstract modified)

**002796** Hall, C. E.; Nasseth, D. Dept. of Physiology and Biophysics, University of Texas Medical Branch, Galveston, TX 77550 **Factors affecting the acute pressor response to bolus cadmium injections.** Physiology & Behavior. 24(2):373-380, 1980.

Cadmium chloride (1 or 2mg/kg) induced pressor responses in conscious or anesthetized female Sprague-Dawley rats when administered ip, iv, or subcutaneously, but not orally. Pressor responses to cadmium were generally not observed in male Sprague-Dawley, Fischer-344, SHR, or WKY rats at 5 weeks of age. Pressor responses were observed in conscious or unconscious Sprague-Dawley and Fischer-344 rats and in unconscious SHR and WKY rats at 6 to 10 weeks of age. 49 references. (Author abstract modified)

**002797** Hammer, Rudolf; Kobinger, Walter; Pichler, Ludwig. Kobinger: Ernst Boehringer Institut fur Arzneimittelforschung A-1121 Vienna, Dr. Boehringer Gasse 5-11, Austria **Binding of an imidazolidine (clonidine), an oxazoloazepin (B-HT 933) and a thiazoloazepin (B-HT 920) to rat brain alpha-adrenoceptors and relation to cardiovascular effects.** European Journal of Pharmacology. 62(4):277-285, 1980.

The specific binding of clonidine to alpha-adrenoceptors in male Chbb:THOM rat brain was compared to that of the oxazoloazepin B-HT 933 and the thiazoloazepin B-HT 920. The effects of these drugs on blood pressure in spinal animals and on bradycardia in vagotomized animals were also determined. Clonidine, B-HT 920, and B-HT 933 showed decreasing order of potency in all three tests. Results demonstrate the similarity of alpha-adrenoceptors in brain membranes, peripheral vascular sites, and central sympathoinhibitory sites. 16 references. (Author abstract modified)

**002798** Harik, Sami I.; Sharma, Virendra K.; Wetherbee, John R.; Warren, Robert H.; Banerjee, Shailesh P. Dept. of Neurology (D 4-5), University of Miami School of Medicine, P. O. Box 016960, Miami, FL 33101 **Adrenergic receptors of cerebral microvessels.** European Journal of Pharmacology. 61(2):207-208, 1980.

The binding of 3H-dihydroalprenolol in cerebral microvessel preparations from rats and pigs demonstrated the presence of beta-adrenergic receptors. No appreciable binding to alpha-adrenergic receptors in microvessel preparations was detected in 3H-WB-4101 binding assay. The demonstration of beta-adrenergic receptors in brain microvessels indicates the brain microvasculature may be influenced by its noradrenergic innervation. 5 references.

**002799** Harper, Barbara; Hughes, I. E. Dept. of Pharmacology, Medical and Dental Building, University, Leeds LS2 9JT, England **Presynaptic alpha-adrenoceptor blocking properties among tri- and tetra-cyclic antidepressant drugs.** British Journal of Pharmacology. 67(4):511-517, 1979.

In mouse vas deferens preloaded with (3H)-(-)-noradrenaline, the antidepressants mianserin and ORG-GC-94 produced a concentration dependent increase in electrically evoked overflow of tritium and in contractile response to electrical stimulation. High concentrations also slightly increased resting release of tritium. These effects were not significantly altered by cocaine in concentrations large enough to block noradrenaline uptake. The two drugs also antagonized the inhibitory effect of clonidine on the twitch response, reduced the inhibitory effect of exogenous (-)-noradrenaline on evoked overflow, and reduced the ability of phentolamine to increase evoked overflow and contractile response. Maprotiline, desipramine, and nortriptyline produced parallel declines in evoked tritium overflow and in contractile response but increased resting overflow at high concentrations. Doxepin, imipramine, and iprindole all increased resting overflow at high concentrations, but produced only small changes in evoked overflow and contractile response at lower concentrations. Results suggest that mianserin and ORG-GC-94 produce a blockade of presynaptic alpha-adrenoceptors that may contribute to their antidepressant effects but is not common to all antidepressants. 14 references. (Author abstract modified)

**002800** Heath, Robert G.; Fitzjarrell, A. T.; Garey, R. E.; Myers, W. A. Dept. of Psychiatry and Neurology, Tulane University School of Medicine, New Orleans, LA 70118 **Chronic marihuana smoking: its effect of function and structure of the primate brain.** In: Nahas, G., Marihuana: biological effects. Oxford, Pergamon, 1979. 777 p. (p. 713-730).

The effects of chronic marihuana smoking on the function and structure of the primate brain was studied in monkeys. Studies are described which clarify two issues that provoked criticism in previous research: 1) that the effects reported resulted from excessive exposure to smoke resulting in anoxia and were not attributable to psychoactive cannabis derivatives; and 2) that dosages of cannabis used were far in excess of those used by human subjects. Acute effects on brain function that were obtained in monkeys with chronically implanted deep electrodes and tested with cannabis derivatives other than delta9-tetrahydrocannabinol are described. In addition, data from ongoing electron microscopic studies on the brains of monkeys exposed to cannabis derivatives is presented. 16 references.

**002801** Heidler, I.; Mares, J.; Trojan, S. Institute of Physiology, Medical Faculty, Prague 2, Albertov 5, Czechoslovakia **Influence of Rivotril (clonazepam) on the spontaneous EEG in rats.** Activitas Nervosa Superior. 21(1):13-14, 1979.

The effects of Rivotril (clonazepam) a new benzodiazepine with strong antiepileptic effects, on the spontaneous ECoG of 40 adult male rats were examined. Slow high waves as well as activity 10 to 13 Hz with high amplitude waves were observed following i.p. clonazepam. The time course of the changes of ECoG after the administration of clonazepam indicates that the effects of all the doses tested reach their maximum and stabilize within 9 minutes. 5 references.

**002802** Heikkila, John J.; Brown, Ian R. Dept. of Zoology, Scarborough College, University of Toronto, West Hill, Ontario M1C 1A4, Canada **Disaggregation of brain polysomes after LSD in vivo: involvement of LSD-induced hyperthermia.** Neurochemical Research. 4(6):763-776, 1979.

The involvement of LSD-induced hyperthermia in the brain specific disaggregation of polysomes caused by intravenous administration of LSD to rabbits was investigated. Both LSD-induced hyperthermia and brain polysome disaggregation were found to increase in parallel under conditions which accentuated the effect of the drug on brain protein synthesis. Pretreatment with neurotransmitter receptor blockers or placing the animal at an ambient temperature of 4 degrees C after LSD administration prevented both hyperthermia and brain polysome disaggregation. The administration of apomorphine, which causes hyperthermia in rabbits also caused disaggregation of brain polysomes. Direct elevations of the body temperature to levels similar to that found after LSD was achieved by placing animals at an ambient temperature of 37 degrees C. Under these conditions, a brain specific disaggregation of polysomes resulted which was not due to RNAase activation. After either LSD or direct heating, the brain polysome shift was associated with a relocalization of polyadenylated mRNA from polysomes to monosomes as determined by (3H)polyuridylate hybridization. Since poly-

some disaggregation was found only in brain, it appears that the brain may be more sensitive to elevations in body temperature compared to other organs. 25 references. (Authorabstract modified)

002803 Heinz, Gary H.; Hill, Elwood F.; Contrera, Joseph F. Patuxent Wildlife Research Center, Laurel, MD 20811 **Dopamine and norepinephrine depletion in ring doves fed DDE, dieldrin, and Aroclor 1254.** Toxicology and Applied Pharmacology. 53(1):75-82, 1980.

Levels of dopamine and norepinephrine in the brains of ring doves were compared for those fed a control diet or a diet containing 2, 20, or 200 ppm DDE, 1, 4, or 16 ppm dieldrin, or 1, 10, or 100 ppm Aroclor 1254. Levels of dopamine and norepinephrine were measured in half of each brain, and levels of DDE, dieldrin, or Aroclor 1254 were determined in the other half. The intermediate and high levels of each chemical caused depletions in both neurotransmitters, and brain residues of each chemical were negatively correlated with levels of neurotransmitters. The highest concentrations of DDE, dieldrin, and Aroclor 1254 depressed averages of dopamine to 42.4, 41.4, and 45.2% of control level and norepinephrine to 61.6, 62.0, and 56.9% of controls, respectively. Depletions of dopamine and norepinephrine could result in abnormal behavior of contaminated birds in the wild, and the detection of such depletions could become an important tool in assessing contaminant-induced behavioral aberrations in birds. 36 references. (Author abstract)

002804 Hennig, Charles W.; Harston, Craig T.; Dunlap, William P. Division of Science and Mathematics, Centre College of Kentucky, Danville, KY 40422 **Blockade of the melatonin potentiation of tonic immobility in chickens by methysergide and cyproheptadine.** Behavioral and Neural Biology. 29(3):372-377, 1980.

The effects of two antiserotonergic drugs, methysergide and cyproheptadine, on tonic immobility in chickens were examined. Methysergide increased the number of inductions required to produce immobility, while cyproheptadine had no effect on this measure. Neither drug had any significant effect on the duration of immobility under normal conditions, but methysergide significantly reduced the prolongation of immobility duration produced by injections of melatonin. In this regard cyproheptadine had much less of an effect than methysergide. Results are discussed in terms of implications for the serotonergic, midbrain raphe model of tonic immobility and the possible mode of action by melatonin on the immobility response. 10 references. (Author abstract)

002805 Herrling, Paul L.; Hull, Chester D. Pharmaceutical Division, Preclinical Research, Sandoz, Ltd., CH-4002 Basel, Switzerland **Iontophoretically applied dopamine depolarizes and hyperpolarizes the membrane of cat caudate neurons.** Brain Research. 192(2):441-462, 1980.

Dopamine (DA) was applied iontophoretically on intracellularly recorded cat caudate neurons. When ejected 100mcm from the cell soma, DA caused slow depolarizations of the membrane and reduced ongoing firing rate. When DA was applied nearer the soma (about 50mcm away) 70% of the neurons continued to display depolarization, but 30% showed hyperpolarization accompained by reduced firing rate. If DA was applied for prolonged periods on these cells, the initial hyperpolarization was followed by slow depolarization. None of the 74 responsive neurons showed an increased firing rate when DA was ejected continuously or in short pulses. 54 references. (Author abstract modified)

002806 Hexum, Terry D.; Fried, Ranier. Dept. of Pharmacology, University of Nebraska Medical Center, Omaha, NB 68105 **Effects of superoxide radicals on transport (NaK) adenosine triphosphatase and protection by superoxide dismutase.** Neurochemical Research. 4(1):73-82, 1979.

Membrane sodium and potassium activated adenosine triphosphatase (NaK-ATPase) isolated from rat brain was preincubated in a medium in which superoxide radicals were generated enzymatically. Exposure to superoxide radicals caused an irreversible inactivation, which could be prevented by further addition of superoxide dismutase. The NaK-ATPase was also protected by addition of allopurinol, a xanthine oxidase inhibitor, during preincubation. The potassium activated nitrophenylphosphatase associated with NaK-ATPase was also inactivated by preincubation with superoxide radicals, and this effect was prevented by superoxide dismutase. The possible participation of superoxide radicals in the activation of chlorpromazine or in its inhibitory effect on NaK-ATPase is discussed. 28 references. (Author abstract modified)

002807 Heydorn, William E.; Mendels, Joe; Frazer, Alan. Dept. of Pharmacology, University of Pennsylvania, Philadelphia, PA 19104 **Effects of darkness and of desmethylimipramine on pineal gland concentrations of adenosine 3',5'-monophosphate.** Biochemical Pharmacology. 29(10):1341-1346, 1980.

The effects of darkness and of desmethylimipramine (DMI) on pineal gland concentrations of adenosine 3', 5'-monophosphate (cAMP) were investigated. Concentrations of cAMP in the pineal glands of rats exposed to constant light for 7 days and then placed in darkness for up to 3 hours was no different from that measured in the pineal glands of rats kept in constant light. However, if the norepinephrine reuptake inhibitor DMI was injected into rats 1 hour before placing them in the dark, then exposure to darkness caused a rapid, sustained increase in pineal gland concentrations of cAMP. While bilateral adrenal demedullation did not prevent the increase in pineal cAMP in rats treated with DMI and exposed to darkness, bilateral superior cervical ganglionectomy abolished completely the darkness induced rise in cAMP in DMI treated rats. Furthermore, prior treatment of rats with the beta-adrenergic antagonist propranolol prevented the darkness-induced increase in cAMP in rats treated with the inhibitor of norepinephrine reuptake. It appears that increases in sympathetic activity to the pineal gland, induced by darkness, can raise the concentration of cAMP in the gland but only when norepinephrine reuptake is prevented. 35 references. (Author abstract modified)

002808 Hirschhorn, Ira D.; Makman, Maynard H.; Gardner, Eliot L. Dept. of Biochemistry, Albert Einstein College of Medicine, Bronx, NY 10461 **Changes in guanine nucleotide sensitive and insensitive 3H-ADTN binding in striatum following substantia nigra lesions.** European Journal of Pharmacology. 62(1):123-124, 1980.

The effects of unilateral lesions of the substantia nigra on guanine nucleotide sensitive and insensitive 3H-(2-amino-6,7-dihydroxyl-1,2,3,4-tetrahydronaphthalene (3H-ADTN) binding in the striatum of male Sprague-Dawley rats were examined. Specific 3H-ADTN binding was greater in the lesioned striata than in intact striata. The increase was greater in the component sensitive to guanine nucleotide than in the insensitive component, but this difference was not significant. 5 references.

002809 Hodge, Charles J., Jr.; Woods, Charles I.; Delatizky, Jonathan. Dept. of Neurosurgery, State University of New York, Upstate Medical Center, Syracuse, NY 13210 **Noradrenalin, serotonin, and the dorsal horn.** Journal of Neurosurgery. 52(5):674-685, 1980.

The actions of noradrenalin and serotonin in the dorsal horn of cats were studied. L-dopa was given intravenously to cats to cause the release of noradrenalin and 5-HT. The resultant ef-

fects on the response of dorsal horn cells to innocuous and noxious thermal stimulation of skin were determined. It was found that noradrenalin facilitates the responses of dorsal horn cells to innocuous cutaneous stimuli, and has an inhibitory effect on the responses to noxious stimuli. Serotonin inhibits the responses of dorsal horn cells that respond to noxious stimuli, to both innocuous and noxious stimuli. The results are discussed in light of current developments concerning aminergic control of segmental sensory processing. 83 references. (Author abstract modified)

**002810** Hoffman, Andrew R.; Sastry, B. V. Rama; Axelrod, Julius. Pharmacology-Toxicology Program, NIGMS, NIH, Bethesda, MD 20205 **Formation of alpha-methyldopamine ( from p-hydroxyamphetamine by rat brain microsomes.** Pharmacology. 19(5):256-260, 1979.

The in vitro synthesis of alpha-methyldopamine (catecholamphetamine) from p-hydroxyamphetamine by a microsomal enzyme in male Sprague-Dawley rat brain was demonstrated, using a sensitive radioenzymatic assay which couples the formation of the catecholamphetamine to rapid O-methylation by catechol-O-methyltransferase in the presence of (3H)-methyl-S-adenosylmethionine. Results showed that rat brain microsomes contain a cytochrome P-450 dependent monooxygenase that synthesizes catecholamphetamine from p-hydroxyamphetamine, a major metabolite of amphetamine. The formation of the catechol metabolite may be involved in the development of tolerance during chronic amphetamine use. 13 references. (Author abstract modified)

**002811** Hoffman, Douglas W.; Vernadakis, Antonia. Dept. of Pharmacology, University of Colorado School of Medicine, Denver, CO 80262 **Biochemical characterization of (3H)norepinephrine uptake in dissociated brain cell cultures from chick embryos.** Neurochemical Research. 4(6):731-746, 1979.

The uptake of (3H)norepinephrine ((3H)NE) was studied in dissociated brain cell cultures prepared from 8-day-old chick embryos using the whole brain (minus optic lobes). Uptake of (3H)NE, .000000005M, 10 min incubation, in freshly dissociated noncultured embryonic chick brain cells, was detected in 6 day old embryos; it was temperature and drug (cocaine, metanephrine) sensitive and increased with brain development. In cultured cells, which were assayed at various days in culture, the increase in (3H)NE accumulation per culture was less than that seen in freshly dissociated noncultured embryonic cells. When (3H)NE uptake was expressed per mg protein, a decrease with days in culture was observed, reflecting perhaps, a dilution of growth or proliferation of cells not accumulating NE. Metanephrine, .000005M, an inhibitor of extraneuronal uptake, inhibited (3H)NE in 5 day old cultures whereas desmethylimipramine, an inhibitor of neuronal uptake, inhibited (3H)NE in 15 and 20 day old cultures. Cocaine, another neuronal inhibitor, inhibited (3H)NE at 10 and 15 days only. Results are interpreted as suggesting that during early growth in culture, most neuroblasts accumulate NE nonspecifically and, as neuronal maturation proceeds, NE accumulation becomes specific. 32 references. (UTHOR ABSTRACT)

**002812** Holaday, John W.; Faden, Alan I. Dept. of Medical Neurosciences, Division of Neuropsychiatry, Walter Reed Army Institute of Research, Washington, DC 20012 **Naloxone acts at central opiate receptors to reverse hypotension, hypothermia and hypoventilation in spinal shock.** Brain Research. 189(1):295-300, 1980.

The effects of naloxone on blood pressure, respiration, and temperature were studied in male Sprague-Dawley rats after C-7 spinal transection. Results showed that naloxone ameliorates the hypotension, hypothermia, and hypoventilation normally observed in spinal shock. These effects appeared to be mediated by a blockade of endorphin effects at central opiate receptors. 19 references.

**002813** Honma, K.; Hohn, K.-G.; Wuttke, W. Wuttke: Max-Planck-Institute for Biophysical Chemistry, Dept. of Neurobiology, 34 Gottingen-Nikolausberg, Am Fassberg, Germany **Involvement of catecholamines in eliciting LH peaks in 15-day-old female rats: effects of treatment with prolactin.** Brain Research. 179(2):271-279, 1979.

Regional brain catecholamine turnover and serum LH levels were determined in 15-day-old female Sprague-Dawley rats, before and after treatment with prolactin. Norepinephrine (NE) turnover in the medial preoptic areas (MPO) was significantly higher in rats with high serum LH levels than in those with low serum LH. An inverse correlation between LH levels and NE turnover was demonstrated in the posterior mediobasal hypothalamus (PMBH). Serum LH was not correlated with NE turnover in the anterior mediobasal hypothalamus (AMBH) or with dopamine (DA) turnover in any of the three areas examined. Serum FSH and prolactin levels were high in animals with high LH levels. These findings were similar to those obtained in adult proestrous rats, suggesting the LH peaks in 15-day-old rats reflect positive feedback action of estradiol. When ovine prolactin was administered on days 8 to 15, serum LH levels were depressed to barely detectable values; DA turnover increased in the MPO, AMBH, and PMBH, but NE turnover was not altered. Results indicate that DA turnover of the incertohypothalamic and tuberoinfundibular neurons is accelerated by prolactin and that increased DA turnover in one of these systems is responsible for inhibition of LH release. 33 references. (Author abstract modified)

**002814** Hook, Vivian Y. H.; Lee, Nancy M.; Loh, Horace H. Dept. of Pharmacology, University of California, San Francisco, CA 94143 **Partial purification of nuclear protein kinase from small dense nuclei of mouse brain and the effect of chronic morphine treatment.** Journal of Neurochemistry. 34(5):1274-1279, 1980.

To determine whether or not nuclear protein kinase activity may be responsible for the change in phosphorylation of chromatin proteins during morphine tolerance/dependence, the nuclear protein kinases from small dense nuclei of mouse brain have been partially purified by ammonium sulfate fractionation and phosphocellulose column chromatography. Two peaks of cyclic AMP independent nuclear protein kinase activity are eluted from the phosphocellulose column by a linear NaCl gradient. During morphine tolerance/dependence, the specific activity of peak I, but not of peak II, is increased significantly relative to placebo controls. This increase in nuclear protein kinase activity may partially account for the elevated chromatin protein phosphorylation in small dense nuclei of mouse brain seen during morphine tolerance/dependence. 11 references. (Author abstract)

**002815** Hornung, R.; Presek, P.; Glossmann, H. Pharmakologisches Institut der Justus-Liebig-Universitat Giessen, Frankfurter Strasse 107, D-6300 Lahn-Giessen 1, Germany **Alpha adrenoceptors in rat brain: direct identification with prazosin.** Naunyn-Schmiedeberg's Archives of Pharmacology. 308(3):223-230, 1979.

The binding of tritiated prazosin to rat brain membranes was examined. Prazosin binding sites had an association constant of 2nM with optimal binding at pH 7.0. The density of prazocin binding sites was 33fmoles/mg protein, and the half time of dissociation was 7 minutes at 30 degrees. Binding inhibition studies revealed the following descending order of potency for agonists:

naphazoline, clonidine, adrenaline, noradrenaline, phenylephrine, alpha-methylnoradrenaline, dopamine. The descending order of potency for antagonists was: prazosin, phenoxybenzamine, phentolamine, clozapine, yohimbine. Sodium ions, divalent cations, and guanyl nucleotides had little or no effect on binding of the labeled antagonist. Results suggest that labeled prazosin may be a useful tool for characterizing alpha1-adrenoceptors. 23 references. (Author abstract modified)

**002816** Horvath, K.; Jancso, G.; Wollemann, M. Institute of Biochemistry, Biological Research Center, Hungarian Academy of Sciences, Szeged, Hungary **The effect of calcium on the capsaicin activation of adenylate cyclase in rat brain.** Brain Research. 179(2):401-403, 1979.

The adenylate cyclase activity of Wistar rat brain homogenates was examined following incubation with capsaicin or guanyl-5'-ylimidodiphosphate (GppNHp). The activity of the GppNHp pretreated preparation was significantly higher than that of controls. GppNHp increased capsaicin stimulation in the absence of calcium ions (Ca2), but not in the presence of Ca2. When the homogenate was treated with capsaicin in the presence of Ca2, adenylate cyclase activity was also enhanced, but Ca2 alone had no stimulatory effect. 12 references.

**002817** Hosli, E.; Hosli, L. Hosli, L.: Dept. of Physiology, University of Basel, Vesalgasse 1, CH-4051 Basel, Switzerland **Autoradiographic localization of 3H-GABA and 3H-muscimol binding in rat cerebellar cultures.** Experimental Brain Research. 38(2):241-243, 1980.

Autoradiographic techniques were used to study the binding of 3H-GABA and 3H-muscimol in cultures of newborn rat cerebellum. Binding sites for both substances were observed on many cerebellar neurons, such as Purkinje cells and interneurons, but not on glial cells. Binding of 3H-GABA and 3H-muscimol was inhibited by unlabeled GABA and by bicuculline. (Author abstract modified)

**002818** Howland, Richard D.; Vyas, Ivy L.; Lowndes, Herbert E. Dept. of Pharmacology, College of Medicine and Dentistry of New Jersey, New Jersey Medical School, Newark, NJ 07103 **The etiology of acrylamide neuropathy: possible involvement of neuron specific enolase.** Brain Research. 190(2):529-535, 1980.

The effect of monomeric acrylamide, a potent neurotoxic agent, on total and neuron specific enolase activity was studied in vitro and in vivo. Acrylamide completely inhibited total enolase activity of rat brain soluble fractions. In rats chronically treated with acrylamide and exhibiting marked symptoms of neurotoxicity, neuron specific enolase activity was not detectable in sciatic nerves and was only 60% of control activity in brain. Total enolase activity in both central and peripheral nervous tissues was unchanged from control. It is suggested that inhibition of neuron specific enolase may be an important factor in the development of acrylamide neuropathy by interfering with glycolysis in neuronal tissue. 29 references. (Author abstract modified)

**002819** Huang, Li-Yen Mae; Barker, Jeffery L. Laboratory of Neurophysiology, NINCDS, National Institutes of Health, Bethesda, MD 20205 **Pentobarbital: stereospecific actions of () and (-) isomers revealed on cultured mammalian neurons.** Science. 207(4427):195-197, 1980.

The effects of stereoisomers of the barbiturate anesthetic pentobarbital on mouse spinal neurons growing in tissue culture were studied. Intracellular recordings of neuronal membrane properties revealed that the () and (-) isomers caused direct changes in membrane potential and conductance on some but not all of the cells tested. The action of the () isomer was predominantly excitatory, whereas the (-) isomer produced predominantly inhibitory responses. The (-) isomer was considerably more effective in potentiating inhibitory responses to the transmitter gamma-aminobutyric acid. The results show that pentobarbital has multiple effects on neuronal excitability and demonstrates the presence of stereospecific sites of barbiturate action on central neurons. 37 references. (Author abstract)

**002820** Hucker, H. B.; Balletto, A. J.; Zacchei, A. G.; Arison, B. H. Dept. of Drug Metabolism, Merck Institute for Therapeutic Research, West Point, PA 19486 **Metabolism of protriptyline by rabbit liver in vitro.** Pharmacology 19(5):278-281, 1979.

Mass spectrometry and nuclear magnetic resonance analysis were used to identify metabolites of the tricyclic antidepressant protriptyline in a rabbit liver microsomal system. Results showed that about 40% of the added protriptyline was converted to its hydroxylamine metabolite. This biotransformation of protriptyline to its hydroxylamine analog in a rabbit liver microsomal system is believed to be the first demonstration of such a pathway for a tricyclic antidepressant drug. 9 references. (Author abstract modified)

**002821** Hunter, E. G.; Frank, G. B. Dept. of Pharmacology, University of Alberta, Edmonton, Alberta, Canada **An opiate receptor on frog sciatic nerve axons.** Canadian Journal of Physiology and Pharmacology. 57(10):1171-1174, 1979.

The effect of meperidine on the action potential of frog sciatic nerve was examined, using the dobule sucrose gap technique. Meperidine decreased the amplitude, maximum rate of depolarization, and maximum rate of repolarization of the action potential, but had no effect on the resting potential. The depression in amplitude and maximum rate of rise was partially blocked by naloxone, but the maximum rate of depolarization was further depressed. Results suggest that meperidine exerts a nonspecific local anesthetic-like effect as well as an opiate receptor mediated effect. 9 references. (Author abstract modified)

**002822** Hwang, Bang-Hsiung. University of Iowa **Neurotoxin-induced plasticity in catecholaminergic pathways of the rat brainstem. (Ph.D. dissertation).** Dissertation Abstracts International. 39(12):5702-B, 1979. Ann Arbor, Univ. Microfilms No. 7912862, 212p., 1978.

Sprouting responses were investigated in catecholaminergic (CA) fibers in rat brainstem using fluorescence and electron microscopy after neurotoxin treatment. Administration of 6-hydroxydopamine (6-OHDA) into the right lateral ventricle had greater degenerative effects than 5,7-DHT, which appeared to induce greater proliferation of CA fiber sprouts. Collateral sprouts were manifest by 4 days postlesion; and by 8 weeks postlesion, the number of collateral sprouts had decreased indicating a subsequent abortive response by most of the sprouts. CA fibers in the paraventricular nucleus (PAR), periventricular nucleus (PER), dorsomedial nucleus (DM), and the supraoptic commissure (SOC) of the hypothalamus were also studied in young rats following 6-OHDA injection. The restoration of CA fibers at the 6 month stage was found to be 96% of control values in SOC, 79% in PAR and PER, and 68% in DM. Factors responsible for this difference of plasticity were not ascertained. Effects of age on plasticity response in the PAR, PER, SOC, and DM were also found, with restoration of terminals being more rapid and complete in rats lesioned in the neonatal period as compared with those lesioned as adults. (Journal abstract modified)

**002823** Ichida, Seiji; Yonehara, Norifumi; Watanabe, Yasuhiro; Yoshida, Hiroshi. Dept. of Toxicology, Faculty of Pharmacy, Kinki University, Higashi-Osaka 577, Japan **Inhibitory effect of dibutyryl cyclic GMP on potassium-stimulated 45Ca uptake by**

**synaptosomes from rat brain.** Brain Research. 192(2):487-494, 1980.

The potassium stimulated uptake of 45Ca by a P2 synaptosomal fraction from male Sprague-Dawley rat brain was inhibited by dibutyryl cyclic GMP, but not by dibutyryl cyclic AMP. Dibutyryl cyclic GMP did not alter 45Ca uptake in media with low potassium concentrations. The inhibitory effect of dibutyryl cyclic GMP decreased when the concentration of calcium in the medium was increased from 0.1mM to 1mM. Results suggest that cyclic GMP inhibits the calcium influx resulting from depolarization of nerve endings in situ. 29 references. (Author abstract modified)

**002824** Ishikawa, Toshio; Yamamoto, Minoru. Dept. of Physiology and Biochemistry, School of Nursing, Chiba University, Chiba 280, Japan **Involvement of the cholinergic mechanism in depression of the caudate spindle.** Japanese Journal of Pharmacology. 29(3):399-403, 1979.

The involvement of cholinergic and catecholaminergic mechanisms in the caudate spindle recorded from the anterior and posterior sigmoid gyri was examined in cats. The caudate spindle was abolished by physostigmine (0.01 to 0.1mg/kg i.v.) and inhibited by high frequency stimulation of the mesencephalic reticular formation. Both inhibitory effects were antagonized by atropine. The caudate spindle was not altered by L-DOPA (25 to 50mg/kg i.v.), L-DOPA in combination with a monoamine oxidase inhibitor, or methamphetamine (0.5 to 5mg/kg i.v.). Results suggest that a cholinergic rather than catecholaminergic mechanism is involved in depression of the caudate spindle. 8 references. (Author abstract modified)

**002825** Jackler, Frances Ruth. City University of New York **Differential effects of morphine on central mechanisms of reward as assessed by intracranial self-stimulation. (Ph.D. dissertation).** Dissertation Abstracts International. 40(1):484-B, 1979. Ann Arbor, Univ. Microfilms No. 7913137, 415p., 1979.

The differential effects of morphine on central mechanisms of reward as assessed by intracranial self-stimulation were examined with rats. Rats were implanted with dorsal brainstem (DB) and hypothalamic (HYP) electrodes. Most animals showed differences in patterns in the time course of effects at the two electrodes. In several animals, the DB electrode seemed to react as though it has received a functionally higher morphine dose than the corresponding HYP electrode; the DB electrode appeared comparatively more likely to show significant depressant effects and less likely to display facilitative effects. It is concluded that morphine has a facilitative effect on central reward mechanisms and has differential effects within the reward systems. (Journal abstract modified)

**002826** Jaim-Etcheverry, Guillermo; Zieher, Luis Maria. Instituto de Biologia Celular, Buenos Aires, Argentina **DSP-4: a novel compound with neurotoxic effects on noradrenergic neurons of adult and developing rats.** Brain Research. 188(2):513-523, 1980.

The effects of N-(2-chloroethyl)-N-ethyl-2-bromobenzylamine hydrochloride (DSP-4) on central and peripheral noradrenergic neurons were studied in Wistar rats. When given perinatally, DSP-4 did not alter the development of peripheral noradrenergic neurons, but did cause permanent changes in regional brain noradrenaline (NA) levels. The regional changes in brain NA levels seen in rats treated with DSP-4 at birth differed somewhat from those observed in rats treated with DSP-4 as adults, but were similar to those seen in rats treated neonatally with 6-hydroxydopamine. 18 references. (Author abstract modified)

**002827** Jancso, G.; Jancso-Gabor, Aurelia. Dept. of Anatomy, University Medical School, P.O.B. 512, H-6701 Szeged, Hungary **Effect of capsaicin on morphine analgesia -- possible involvement of hypothalamic structures.** Naunyn-Schmiedeberg's Archives of Pharmacology. 311(3):285-288, 1980.

The possible involvement of hypothalamic structures in the effect of capsaicin on morphine analgesia was investigated. Rats were treated with 50mg/kg capsaicin on the second day of life or at the age of 2 to 3 months. The effect of morphine on the nociceptive threshold, as determined by the reaction time in a tail withdrawal test, was measured 3 to 4 months and 1 to 2 months after capsaicin pretreatment, respectively. The analgesic effect of morphine was markedly attenuated in rats treated with capsaicin in the adult age, while neonatal capsaicim treatment did not affect morphine analgesia. Pretreatment of adult rats with capsaicin resulted in the impairment of certain hypothalamic preoptic neurons, while neonatal capsaicin treatment induced selective degeneration of chemosensitive primary sensory neurons without affecting hypothalamic neurons. Therefore, it is suggested that in the analgesic effect of morphine the capsaicin sensitive neurons of the preoptic area are involved, and the contribution of spinal mechanisms might be of minor importance. Thus, the preoptic region may be an important link in endogenous pain controlling systems. 18 references. (Author abstract modified)

**002828** Johnson, Stephen M.; North, R. Alan. North: Neurophysiology Laboratory, Dept. of Pharmacology, Loyola University Stritch School of Medicine, Maywood, IL 60153 **Membrane potential changes in neurones undergoing withdrawal from opiates.** Brain Research. 190(2):559-563, 1980.

Changes in pieces of ileum from guinea pigs induced by chronic morphine exposure were examined using intracellular recording. The opiate antagonist naloxone caused a depolarization of the membrane of cells which had been incubated with morphine for 24 hours. It appears that the morphine sensitive neurons themselves undergo adaptive changes in the continuing presence of morphine. The initial inhibitory effects of morphine pass off, but the dependence of the neuron on the continued presence of morphine is evidenced by its enhanced excitability when the opiate is abruptly displaced. It is concluded that similar changes occurring in single neurons of the central nervous system might underlie the well-known clinical observations that many of the stigmata of opiate withdrawal are opposite in direction and more marked in degree than the initial acute effects of administering an opiate to a naive subject. 29 references.

**002829** Jones, D. L.; Mogenson, G. J. Dept. of Physiology, University of Western Ontario, London, Ontario N6A 5C1, Canada **Nucleus accumbens to globus pallidus GABA projection: electrophysiological and iontophoretic investigations.** Brain Research. 188(1):93-105, 1980.

The presence of a GABA inhibitory projection from the nucleus accumbens to the ventral medial portion of the globus pallidus was demonstrated in male Wistar rats. Neurons in the nucleus accumbens were activated antidromically by electrical stimulation of the globus pallidus. Cells in the globus pallidus were inhibited by electrical stimulation of the nucleus accumbens. Iontophoretic application of picrotoxin attenuated or abolished the inhibitory effect of electrical stimulation of the nucleus accumbens. 31 references.

**002830** Jordan, Larry M.; Pratt, Carol A.; Menzies, John E. Dept. of Physiology, University of Manitoba, Faculty of Medicine, Winnipeg, Manitoba R3E OW3, Canada **Locomotion evoked by brain stem stimulation: occcurrence without phasic segmental afferent input.** Brain Research. 177(1):204-207, 1979.

Stimulation of the mesencephalic locomotor region (MLR) in the brainstem of anesthetized cats was an effective means of activating the spinal generator for locomotion in the absence of cyclic afferent input. Production of rhythmic discharges in ventral root filaments in reponse to MLR stimulation was not altered by the administration of a paralyzing dose of gallamine triethiodide. Since the ipsilateral ventral roots were cut, it is not likely that activation of motoneurons and subsequent rhythmic Ia afferent input led to the alpha-motoneuron discharges observed in these animals. 22 references.

**002831** Kalin, Ned H.; Cohen, Robert M.; Kraemer, Gary W.; Risch, Samuel C.; Shelton, Steven; Cohen, Michelle; McKinney, William T.; Murphy, Dennis L. NIH Clinical Center, Building 10, Room 3D41, Bethesda, MD 20205 **The dexamethasone suppression test as a measure of hypothalamic-pituitary sensitivity to stress. (Unpublished paper).** Bethesda, MD, NIMH, 1980. 12 p.

Because of the current interest in nonhuman primate models of depression and stress, the question of whether the dexamethasone suppression test might prove to be a useful tool in exploring the central regulation of the hypothalamic-pituitary-adrenal (HPA) system in these animal models of psychopathology was addressed. First, a dose response curve was established for the overnight suppression of plasma cortisol with dexamethasone in rhesus monkeys. Then, in monkeys known to exhibit varying degree of arousal to nasogastric intubation, the dexamethasone feedback responsiveness of each animal's HPA system was correlated with its degree of behavioral arousal as rated during the procedures. No correlation was found between individual differences in rated arousal responses to stress and baseline plasma cortisol. However, the degree of suppression of cortisol by dexamethasone did correlate significantly with individual arousal ratings. Baseline cortisol levels did not correlate with the degree of dexamethasone suppression. The data suggest that the dexamethasone suppression test response may provide a better refelction of individual differences in responsiveness of the hypothalamic-pituitary system to stressful stimuli than do baseline levels. 11 references. (Author abstract modified)

**002832** Karlish, S. J. D.; Beauge, L. A.; Glynn, I. M. Glynn: Physiological Laboratory, University of Cambridge, Cambridge, England **Vanadate inhibits (Na K)ATPase by blocking a conformational change of the unphosphorylated form.** Nature. 282(5736):333-335, 1979.

The mechanism of the inhibition of (Na K)ATPase by vanadate was investigated. Evidence from two experiments is presented which provides strong evidence that vanadate inhibits (Na K)ATPase activity by blocking a conformational change that is thought to follow hydrolysis of the phosphoenzyme. When (Na K)ATPase preparations catalyze the hydrolysis of ATP in the absence of K, the rate limiting step is thought to be the hydrolytic step and not the subsequent conformational change. In the absence of K, the hydrolytic activity of the enzyme is much less sensitive to vanadate. 18 references. (Author abstract modified)

**002833** Kase, Yoshitoshi; Takahama, Kazuo; Hashimoto, Tadatoshi; Kaisaku, Jun; Okano, Yoshiro; Miyata, Takeshi. Dept. of Chemico-Pharmacology, Faculty of Pharmaceutical Sciences, Kumamoto University, 1-5 Ohe-honmachi, Kumamoto 862, Japan **Electrophoretic study of pipecolic acid, a biogenic imino acid, in the mammalian brain.** Brain Research. 193(2):608-613, 1980.

The effect of pipecolic acid (PA) on single unit activities in male Wistar rat brain were examined. The imino acid depressed firing of 88 neurons, excited 2, and did not alter firing of 25 units. All hippocampal pyramidal neurons tested were inhibited. It is suggested that the inhibitory response induced by PA may involve a GABAergic mechanism. 27 references.

**002834** Kato, E.; Kuba, K.; Koketsu, K. Kuba: Dept of Physiology, Saga Medical School, Saga 840-01, Japan **Effects of erabutoxins on the cholinergic receptors of bullfrog sympathetic ganglion cells.** Brain Research. 191(1):294-298, 1980.

The effects of erabutoxins (ETXs) on nicotinic and muscarinic receptors of the bullfrog sympathetic ganglion cells were examined. ETX-a and ETX-b both caused slight but significant reversible inhibitions of the nicotinic response to acetylcholine (ACh). Neither ETX affected the muscarinic ACh receptor. 29 references.

**002835** Katz, R. J.; Roth, K. A.; Schmaltz, K. Mental Health Research Institute, Dept. of Psychiatry, University of Michigan Medical Center, Ann Arbor, MI 48109 **Tail pinch facilitation of self-stimulation in the rat -- dependence upon dopamine and independence of opiates.** Pharmacology Biochemistry and Behavior. 12(3):389-391, 1980.

The dependence upon dopamine and independence of opiates of the phenomenon of tail pinch facilitation of self-stimulation in the rat were investigated. It had been demonstrated previously that adult male Sprague-Dawley rats which are chronically maintained upon a schedule of intracranial reward (ICS) show elevated rates of response after a mild tail pinch. Since both dopamine and opiates have been implicated in the mediation of other stress-induced behavioral alterations, it was speculated that dopamine and/or opiates are involved in the ICS effect. Results replicate the initial finding of tail-pinch-induced facilitation of ICS and demonstrate that while opiate blockade failed to affect ICS response, dopaminergic blockade inhibited the ICS response. These findings suggest neuropharmacological specificity for stress related behavioral change, and further implicate dopamine in stress responses. 9 references. (Author abstract modified)

**002836** Kayaalp, S. Oguz; Neff, Norton H. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Differentiation by ascorbic acid of dopamine agonist and antagonist binding sites in striatum.** Life Sciences. 26(22):1837-1841, 1980.

The effects of ascorbic acid on ligands that apparently bind to dopamine (DA) receptors were investigated. Ascorbic acid, which is usually included in the incubation mixture when studying DA receptor binding sites, was found to inhibit the specific binding of the agonists ADTN and apomorphine but not the antagonists haloperidol and spiroperidol. Other reducing agents have a similar action. This observation is consistent with the notion that DA agonists and antagonists sites are separate and distinct. Morever, results suggest the possibility that the number of agonist sites in vivo may be modulated, in part, by the state of oxidation of the binding sites. 13 references. (Author abstract modified)

**002837** Kerwin, R. W.; Pycock, C. J. Dept. of Pharmacology, Medical School, University of Bristol, Bristol BS8 1TD, England **Role of taurine as a possible transmitter in the thermoregulatory pathways of the rat.** Journal of Pharmacy and Pharmacology. 31(7):466-470, 1979.

Unilateral injection of taurine (10 or 20mcg) into the lateral ventricle of male Porton rats caused an increase in core temperature. Bilateral injection of 2.5 and 5mcg taurine into the preoptic region of the anterior hypothalamus induced a dose related hyperthermia, but a 10mcg dose caused hypothermia. The hyperthermia induced by intrahypothalamic taurine was blocked by pretreatment with strychnine in doses (5 and 15mcg) that

had no effect on core temperature when given alone. Intrahypothalamic injection of hypotaurine also induced hyperthermia, whereas GABA (10mcg) caused hypothermia and glycine (10mcg) had no effect. Potassium (50mM) stimulated release of radioactivity from superfused slices of anterior hypothalamus prelabeled with (3H)taurine, and this effect was calcium dependent. A high affinity uptake mechanism (Km 8.5mcM) was demonstrated for (3H)taurine in slices of anterior hypothalamus. Results suggest that taurine may act as a neurotransmitter in the anterior hypothalamus. 23 references. (Author abstract modified)

**002838** Kinnes, Carolyn Gray; Connors, B.; Somjen, G. Somjen: Dept. of Physiology, Duke University Medical Center, Durham, NC 27710 **The effects of convulsant doses of penicillin on primary afferents, dorsal root ganglion cells, and on inhibition in the spinal cord.** Brain Research. 192(2):495-512, 1980.

Penicillin counteracted the GABA-induced depolarization of dorsal root ganglion cells in rats. A convulsant dose of penicillin also diminished the amplitude of the stimulus evoked dorsal root potential (DRP) in spinal afferent fibers in decapitated cats, but the degree of DRP depression could not be correlated with the intensity of seizure activity. Penicillin enhanced or failed to alter inhibitory reflex effects presumed to be presynaptic. 58 references. (Author abstract modified)

**002839** Klepner, Claire A.; Lippa, Arnold S.; Benson, Donald I.; Sano, Mary C.; Beer, Bernard. CNS Biology, Medical Research Division, Lederle Laboratories, American Cyanamid Company, Middletown Road, Pearl River, NY 10965 **Resolution of two biochemically and pharmacologically distinct benzodiazepine receptors.** Pharmacology Biochemistry and Behavior. 11(4):457-462, 1979.

The existence of two pharmacologically and biochemically distinct populations of benzodiazepine (BDZ) receptors in male Wistar rat brain was demonstrated. Type 1 BDZ receptors showed a high affinity for triazolopyridazines (TPZs) as well as BDZs, were not coupled to GABA receptors or to chloride ionophores, and were implicated in mediation of anxiolytic actions. The type 2 BDZ receptors showed a high affinity for BDZs and a low affinity for TPZs, were coupled to GABA receptors or to chloride ionophores, and were associated with the nonanxiolytic actions of BDZs, such as sedation and ataxia. 28 references. (Author abstract modified)

**002840** Knoll, Joseph. Department of Pharmacology, Semmelweis University of Medicine, 1445 Budapest, POB 370, VIII Nagyvarad ter 4, Hungary **(-)Deprenyl -- the MAO inhibitor without the effect.'** Trends in NeuroSciences. 2(5):111-113, 1979.

The physiological functions of monoamine oxidase (MAO) inhibitors, two forms of MAO, and the development of (-)deprenyl, the first highly potent, irreversible MAO inhibitor without the effect" are discussed. MAO inhibitors are potentially important drugs, especially in the treatment of psychiatric disorders. However, nonspecific MAO inhibitors block the action of the MAO which are involved in detoxifying various amines derived from various foods, especially cheese, allowing these amines to exert a hypertensive reaction (the cheese effect). This has limited the use of MAO inhibitors as therapeutic agents, but the discovery to two types of MAO, and the development of (-)deprenyl may change this situation. 10 references. (Author abstract modified)

**002841** Knych, Edward T.; Eisenberg, Richard M. Dept. of Pharmacology, University of Minnesota, Duluth, MN 55812 **Effect of fluoxetine and metergoline on amphetamine-induced rise in plasma corticosterone.** Life Sciences. 26(18):1489-1496, 1980.

The effect of the serotonin reuptake inhibitor, fluoxetine, and the serotonin antagonist, metergoline, on the rise in plasma corticosterone induced by amphetamine was studied in the conscious, unrestrained rat. Fluoxetine did not affect plasma corticosterone. However, fluoxetine when administered two hours prior to amphetamine, significantly potentiated the amphetamine-induced rise in plasma corticosterone. Fluoxetine had no effect on the response induced by the highest dose of amphetamine utilized in the study. In contrast, metergoline produced a dose dependent increase in plasma corticosterone over the range 0.1 to 5.0 mg/kg. This response reached maximum 30 minutes after drug administration and had a duration of approximately 120 minutes. Pretreatment of animals with metergoline 3 hours before the administration of amphetamine resulted in a significant decrease in the corticosterone rise induced by amphetamine. Lower doses of metergoline were ineffective in reducing the amphetamine-induced response. These observations support the hypothesis that the amphetamine-induced rise in plasma corticosterone is due, in part, to stimulation of serotonergic neurons. 23 references. (Author abstract)

**002842** Kobayashi, Haruo; Yuyama, Akira; Matsusaka, Naonori; Takeno, Kazu; Yanagiya, Iwao. Dept. of Veterinary Pharmacology, Faculty of Agriculture, Iwate University, Morioka 020, Japan **Effect of methylmercury on brain acetylcholine concentration and turnover in mice.** Toxicology and Applied Pharmacology. 54(1):1-8, 1980.

The effects of methylmercury choloride (MMC) on regional acetylcholine (ACh) concentrations and turnover in the mouse brain were studied and compared with those of 3'-chloro-4-stilbazole (CS) and of hemicholinium-3 (HD-3). A long-term treatment with MMC-induced nervous signs and decreased ACh in striatum and cerebral cortex, and conversion ratios of (14C)ACh in cerebellum, striatum, and cerbral cortex of mice. A single administration of CS decreased ACh in the cortex and the conversion ratios in the three brain regions. An intracerebral injection of HC-3 also decreased ACh and the conversion ratios in striatum and cortex. It is postulated that ACh concentration and ACh turnover rate in brain of methylmercury poisoned animals may be reduced. 52 references. (Author abstract modified)

**002843** Koehn, Gary L.; Henderson, Graeme; Karczmar, Alexander G. Dept. of Pharmacology, Loyola University Stritch School of Medicine, Maywood, IL 60153 **Di-isopropyl phosphofluoridate-induced antinociception: possible role of endogenous opioids.** European Journal of Pharmacology. 61(2):167-173, 1980.

Di-isopropyl phosphofluoridate (DFP, 0.1 to 1.5mg/kg) produced antinociceptive responses in male Sprague-Dawley rats in the hotplate test. Naloxone reduced DFP-induced antinociception, but did not affect the attenuated locomotor activity or hypothermia produced by DFP. Animals made tolerant to morphine showed no cross-tolerance to DFP. Antinociception induced by DFP or morphine was antagonized stereoselectively by narcotic antagonists. Results suggest that DFP-induced antinociception is mediated by the release of endogenous opioids, but possibly not from the sites involved in morphine tolerance. 16 references. (Author abstract modified)

**002844** Koide, Tohru; Uyemura, Keiichi. Dept. of Pharmacology, Research Laboratories of Chugai Pharmaceutical Co. Ltd., 41-8, Takada-3-chome, Toshima-ku, Tokyo 171, Japan **Inhibition of (3H)-dopamine uptake into rat brain synaptosomes by the new non-tricyclic antidepressants, FS32 and FS97.** European Journal of Pharmacology. 62(2/3):147-155, 1980.

The effects of the nontricyclic antidepressants, 1-(3-(dimethylamino) -propyl)-5-methyl-3-phenyl-1H-indazole (FS32) and its

N-desmethylated compound FS97, on the uptake of tritiated dopamine (3H-DA) were studied in rat whole brain synaptosomes and striatal synaptosomes. The uptake of 3H-DA into synaptosomes was saturable and temperature and time dependent. The inhibitory activities of the two compounds were comparable to those of amitriptyline, nortriptyline, and iprindole and nearly twice as great as those of imipramine and desipramine. Kinetic studies indicate that FS32 and FS97 were competitive inhibitors of 3H-DA uptake. Neither drug caused a significant release of 3H-DA from the synaptosomes. 33 references. (Author abstract modified)

**002845** Kolb, Vera M. Dept. of Chemistry and Biochemistry, Southern Illinois University, Carbondale, IL 62901 **Long-range substituent effects in morphine-type agonists and antagonists: a possible explanation for some opiate anomalies.** Journal of Pharmaceutical Sciences. 68(10):1250-1254, 1979.

Anomalous substituent effects on the analgesic activity of morphine type opiate agonists and antagonists are discussed. A mechanism is proposed by which substitution into the N-normorphine portion of these drugs alters the activity of the parent molecule. According to this model, a remote substituent distorts the whole molecule via a conformational transmission effect and thereby changes the fit between the opiate and its receptor, the electron density distribution throughout the molecule, the directionality of the lone electron pair on the nitrogen, and the pKa of the drug. 45 references. (Author abstract modified)

**002846** Komiya, Yoshiaki; Kurokawa, Masanori. Dept. of Biochemistry, Institute of Brain Research, Tokyo University Faculty of Medicine, Hongo 7-3-1, Bunkyo ku, Tokyo 113, Japan **Preferential blockade of the tubulin transport by colchicine.** Brain Research. 190(2):505-516, 1980.

Migration of the neurofilament polypeptides, alpha and beta-tubulins and actin in the sciatic nerve and the dorsal root of the adult rat was examined by fluorography. Colchicine injected into the ganglion 10 minutes before methionine preferentially blocked the tubulin transport, with little if any blockade of the polypeptides and actin. In contrast to colchicine, vinblastine sulphate injected into the ganglion in a similar way blocked the transport of all the polypeptides, tubulins and actin. Cytochalasin D had no effect on the slow axoplasmic transport. 24 references. (Author abstract modified)

**002847** Kostrzewa, Richard M.; Fukushima, Hideki; Harston, Craig T.; Perry, Kenneth W.; Fuller, Ray W.; Kastin, Abba J. Dept. of Pharmacology, East Tennessee State University College of Medicine, Johnson City, TN 37601 **Striatal dopamine turnover and MIF-I.** Brain Research Bulletin. 4(6):799-802, 1979.

The actions of the antiparkinsonian agent L-prolyl-L-leucylglycine amide (PLG, MIF-I) on the turnover of striatal dopamine (DA) were examined in a series of experiments. MIF-I failed to alter the rate of decline of endogenous DA in the caudate nucleus of rats pretreated with alpha-methyl-p-tyrosine. In addition, MIF-I did not change endogenous dihydroxyphenylacetic acid or homovanillic acid in rat striatum. These studies indicate that MIF-I does not alter the turnover rate of DA in nigrostriatal neurons. It is possible that MIF-I or some substance released by MIF-I acts at a postsynaptic receptor site. 26 references. (Author abstract modified)

**002848** Koyunchuoglu, H.; Gungor, M.; Eroglu, L.; Sagduyu, H. Dept. of Pharmacology and Clinical Pharmacology, Istanbul Medical Faculty, Capa, Istanbul, Turkey **The antagonizing effect of aspartic acid on morphine withdrawal and levallorphan-precipitated abstinence syndrome signs and on associated changes in brain levels of free amino acids in the rat.** Psychopharmacology. 62(1):89-95, 1979.

Changes in the levels of free amino acids in the brains of white rats from which morphine has been withdrawn after the chronic administration of morphine or morphine plus aspartic acid were investigated. Ss received morphine and aspartic acid separately and in combination in a 5% saccharose solution instead of drinking water for 30 days. Some of the dependent Ss were then withdrawn and others were injected with levallorphan. Flying, jumping, wet dog shaking, body weight loss, and motor activity were estimated and free amino acid levels in the brain were determined. Aspartic acid prevented or antagonized the behavioral signs and the changes in free amino acid level in the brain. (Author abstract modified)

**002849** Koyuncuoglu, H.; Atamer-Simsek, S.; Keyer-Uysal, M. Dept. of Pharmacology, Istanbul Medical Faculty, Capa-Istanbul, Turkey **Effects of continuous and acute administration of small doses of apomorphine, alone or in combination with chlorpromazine, on the brain monoamines and free amino acid levels in the rat.** Psychopharmacology. 66(2):171-177, 1979.

The mutual effect of small doses of apomorphine (AP) and/or chlorpromazine (CPZ) on the brain levels of dopamine (DA), noradrenalin (NA), 5-hydroxytryptamine (5-HT), and free amino acids was investigated. Following the oral administration of a small dose of AP and a therapeutic dose of CPZ (separately and in combination), rats were injected with a small dose of AP. In addition to the partial antagonistic effect of CPZ on the changes in the brain monoamines, an increase in the levels of free amino acids was observed in the brains of the rats after oral administration. The effect of AP injection was reversed in the rats which were given CPZ in combination with oral AP. To make further progress with the problems concerning central acting drugs and pathophysiologic states, it seems necessary to take all the aspects of the brain free amino acids into consideration in the same way as the other neurotransmitters. 25 references. (Author abstract modified)

**002850** Kramis, R.; Vanderwolf, C. H. Dept. of Psychology, University of Western Ontario, London, Ontario N6A 5C2, Canada **Frequency-specific RSA-like hippocampal patterns elicited by septal, hypothalamic, and brain stem electrical stimulation.** Brain Research. 192(2):383-398, 1980.

Hippocampal electrographic patterns comprised of specific frequencies of slow waves similar to normal hippocampal rhythmical slow activity (RSA, theta) were generated by electrical stimulation of specific septal, hypothalamic, and brainstem sites. Waves elicited from some of these sites could be differentiated into atropine sensitive (immobility related) and atropine resistant (movement related) types by the same criteria used to define atropine sensitive and atropine resistant RSA. It was not possible to identify the sites that mediate atropine sensitive and atropine resistant RSA. 26 references. (Author abstract modified)

**002851** Krstic, M. K.; Djurkovic, Draginja. Dept. of Pharmacology, Faculty of Medicine, P. O. Box 662, Belgrade, Yugoslavia **Analysis of cardiovascular responses to central administration of 5-hydroxytryptamine in rats.** Neuropharmacology. 19(5):455-463, 1980.

Central injection of 5-hydroxytryptamine (5-HT) produced an initial increase and subsequent decrease in arterial blood pressure and heartrate, indicating 5-HT participates in the central control of the rat cardiovascular system. The pressor response to intracerebroventricular administration of 5-HT was due to central 5-HT receptor site activation, followed by the release of catecholamines from adrenergic nerve terminals and the adrenal medulla. It is suggested that serotonergic as well as cholinergic transmission may occur in the sympathetic ganglia. 45 references. (Author abstract modified)

**002852** Kubo, T.; Hashimoto, M. Dept. of Pharmacology, Research Laboratories, Fujisawa Pharmaceutical Co., Ltd., Kashima, Yodogawa-ku, Osaka 532, Japan **Effects of intraventricular and intraspinal 6-hydroxydopamine on blood pressure of DOCA-saline hypertensive rats.** Archives Internationales de Pharmacodynamie et de Therapie. 238(1):50-59, 1979.

Intraventricular administration of 6-hydroxydopamine (6-OHDA) prevented the development of hypertension following deoxycorticosterone acetate (DOCA) and saline treatments in male Wistar rats, but did not reverse hypertension once it had developed. The 6-OHDA treatment also reduced salt intake, but its protective effects on blood pressure were not secondary to the salt reduction. The development of DOCA/saline hypertension was not affected by intraspinal pretreatment with 6-OHDA, which produced a complete loss of noradrenaline only in the spinal cord. Results suggest that brain adrenergic neurons may participate in the production of DOCA/salt hypertension, whereas noradrenergic projections in the spinal cord are not essential for the process. 21 references. (Author abstract modified)

**002853** Ladinsky, H.; Consolo, S.; Tirelli, A. S.; Forloni, G. L. Istituto di Richerche Farmacologiche Mario Negri, Via Eritrea, 62, I-20157 Milan, Italy **Evidence for noradrenergic mediation of the oxotremorine-induced increase in acetylcholine content in rat hippocampus.** Brain Research. 187(2):494-498, 1980.

Oxotremorine increased the level of acetylcholine in the female CD1 rat hippocampus, and this effect was blocked by drugs that interfere with noradrenergic function. Drugs that alter dopaminergic or serotonergic function were ineffective. Results suggest that muscarinic activation by oxotremorine triggers an inhibitory feedback on cholinergic neurons via the activation of noradrenergic neurons. 28 references.

**002854** Lange, D. G.; Roerig, S. C.; Fujimoto, J. M.; Wang, R. I. H. Dept. of Pharmacology and Toxicology, Medical College of Wisconsin, Milwaukee, WI 53226 **Absence of cross-tolerance to heroin in morphine-tolerant mice.** Science. 208(4439):72-74, 1980.

Tolerance to morphine and cross-tolerance to heroin were studied in mice in the presence or absence of implanted morphine pellets. Mice implanted with the pellets demonstrated a 30 fold increase in tolerance to subcutaneously administered morphine but showed no cross-tolerance to subcutaneously administered heroin. When given morphine intracerebroventricularly, the mice showed no tolerance to morphine or cross-tolerance to heroin. These observations depended on the presence of the morphine pellet. If the pellets were removed prior to determinations of potency, the expected responses, i.e., tolerance to morphine and cross-tolerance to heroin, were obtained. These observations support a mechanism of tolerance that is based on differential disposition, and suggest that the blood-brain barrier may be the prime site for the expression of tolerance to morphine in mice. The results are discussed in relation to previous conflicting findings. 23 references. (Author abstract modified)

**002855** Langer, Salomon Z.; Raisman, Rita; Briley, Michael S. Dept. of Biology, LERS, Synthelabo, 58 rue de la Glaciere, F-75013 Paris, France **Stereoselective inhibition of 3H-imipramine binding by antidepressant drugs and their derivatives.** European Journal of Pharmacology. 64(1):89-90, 1980.

The stereoselectivity of the 3H-imipramine binding site was demonstrated in rat brain. The inhibition of 3H-imipramine binding by stereoisomers of zimelidine, norzimelidine, and the 10-hydroxy derviatives of amitriptyline and nortriptyline indicated the z-forms were more potent than e-forms. The potency of these compounds in inhibiting 3H-impramine binding was consistent with their clinical potency. 4 references.

**002856** Lassen, J. Buus; Lund, J.; Sondergaard, I. A/S Ferrosan, Dept. of Pharmacology, Sydmarken 1-5, DK-2860 Soeborg, Denmark **Central and peripheral 5-HT uptake in rats treated chronically with femoxetine, paroxetine, and chlorimipramine.** Psychopharmacology. 68(3):229-233, 1980.

Wistar rats were treated for 4 weeks with the 5-hydroxytryptamine (5-HT) uptake inhibitors femoxetine, paroxetine, and chlorimipramine. Femoxetine and paroxetine antagonized the hypermotility and brain 5-HT depletion induced by p-chloroamphetamine (PCA) and depleted blood 5-HT levels. Low plasma concentrations of chlorimipramine inhibited the PCA-induced hypermotility without affecting the PCA depletion of brain 5-HT. 25 references. (Author abstract modified)

**002857** Lee, Nancy M.; Smith, Andrew P. Dept. of Psychiatry, Langley-Porter Neuropsychiatric Institute, University of California, San Francisco, CA 94143 **A protein-lipid model of the opiate receptor.** Life Sciences. 26(18):1459-1464, 1980.

The complexity of the opiate analgesia receptor is examined in a review of the literature concerning the heterogeneity of opiate receptor interactions, the effect of various enzymatic and chemical treatments of brain membranes on opiate binding, and physicochemical properties of detergent extracted membrane components. Based on these findings, a protein lipid model of the opiate receptor is proposed. According the model proposed, the opiate receptor consists of both protein and lipid; the former contains a binding site for enkephalins, and the latter a site for alkaloids, with beta-endorphin interacting with both sites. Implications of the model are discussed. 37 references. (Author abstract modified)

**002858** Lee, Tony J.-F.; Chiueh, Chuang C.; Adams, Maren. Dept. of Pharmacology, Southern Illinois University, School of Medicine, P.O. Box 3926, Springfield, IL 62708 **Synaptic transmission of vasoconstrictor nerves in rabbit basilar artery.** European Journal of Pharmacology. 61(1):55-70, 1980.

Neurogenic vasoconstriction was studied in ring segments of rabbit basilar arteries to determine the identity of the neurotransmitter involved. Results show that neurogenic vasoconstriction of the basilar arteries consists of two components. The initial component was sensitive to phenoxybenzamine (PBZ) and probably due to norepinephrine release. The second phase was resistant to PBZ and apparently mediated by a second, unidentified transmitter. 43 references. (Author abstract modified)

**002859** Leelavathi, Doddamane E.; Smith, Robert C. Smith: Texas Research Institute of Mental Sciences, 1300 Moursund, Texas Medical Center, Houston, TX 77030 **Chronic neuroleptics and brain monoamine oxidase activity.** Biological Psychiatry. 15(3):479-484, 1980.

The effect of chronic administration of haloperidol or fluphenazine on monoamine oxidase (MAO) activity in the rat brain was studied. Nine days after termination of chronic drug administration, rats who had received fluphenazine or haloperidol had significantly lower MAO activity in mitochondrial preparations from rat cortex, and in crude homogenates from rat hippocampus, as compared to chronic saline controls. It is concluded that chronic administration of the drugs inhibits both Type-A and Type-B MAO, but that there is a greater inhibition of the B-form in the mitochondrial preparations from rat cortex. Implications of the findings are discussed. 19 references.

**002860** Lerner, Pauline; Dendel, Peter S.; Major, Leslie F. Section on Biochemistry and Pharmacology, Biological Psychiatry Branch, NIMH, Bethesda, MD 20205 **Dopamine-beta-hydroxylase in cerebrospinal fluid and plasma: effects of alpha-adrenergic agents.** Brain Research. 189(1):183-191, 1980.

The effects of drugs that alter central noradrenergic activity on dopamine-beta-hydroxylase (DBH) activity in cerebrospinal fluid (CSF) and plasma were studied in cats. Phenoxybenzamine significantly increased DBH activity in the CSF. No consistent changes in plasma DBH were seen, but DBH tended to increase from low basal levels and decrease from high basal levels. Clonidine significanlty decreased the DBH activity in CSF, but its effects on plasma DBH were dependent on basal enzyme level. 38 references. (Author abstract modified)

**002861** Levin, W.; Kuntzman, R; Conney, A. H. Dept. of Biochemistry and Drug Metabolism, Hoffmann-La Roche, Inc., Nutley, NJ 07110 **Stimulatory effect of phenobarbital on the metabolism of the oral contraceptive 17alpha-ethynylestradiol-3-methyl ether (mestranol) by rat liver microsomes.** Pharmacology. 19(5):249-255, 1979.

Pretreatment of female Sprague-Dawley rats with phenobarbital for 4 days stimulated the activity of liver microsomal enzymes that metabolize 17alpha-ethynylestradiol-3-methyl ether (mestranol). This effect may account for the decreased uterotropic action of mestranol in rats pretreated with phenobarbital. This finding may also explain unwanted pregnancies in women taking oral contraceptives in combination with phenobarbital or other enzyme-inducing drugs. 36 references. (Author abstract modified)

**002862** Levitt, Lee J.; Quesenberry, Peter J. Division of Hematology-Oncology, University of Virginia, Charlottesville 22903 **The effect of lithium on murine hematopoiesis in a liquid culture system.** New England Journal of Medicine. 302(13):713-719, 1980.

The effect of lithium on murine hematopoiesis in a liquid culture system providing for the prolonged growth of stem cells and their progeny was studied. After 1 week of incubation, lithium, at a supernatant concentration of 1mmol per liter, increased murine pluripotent stem cells to 232% of control values, granulocytemonocyte progenitor cells to 218% of control values, granulocytes to 125% of control values, and megakaryocytes to 246% of control values. These increases were associated with transient elevations in colony stimulatory activity. Prolonged exposure to lithium was associated with a dose dependent progressive depletion of stem cells and their progeny. Lithium enhancement of granulopoiesis may be explained by primary stimulation of the pluripotent stem cells. It is concluded that prolonged proliferative stress induced by lithium when the stem cell reserve is limited may be associated with diminished replicative potential of the stem cells and rapid depletion of cells. 43 references. (Author abstract)

**002863** Lin, M. T.; Chandra, A.; Su, C. Y. Dept. of Physiology and Biophysics, National Defense Medical Center, Taipei, Taiwan **Naloxone produces hypothermia in rats pretreated with beta-endorphin and morphine.** Neuropharmacology. 19(5):435-441, 1980.

Thermoregulatory responses to naloxone were studied in male Sprague-Dawley rats pretreated with saline, morphine, or beta-endorphin. In the saline group, morphine and beta-endorphin produced catatonia, sedation, and hypothermia due to decreased metabolic rate and cutaneous vasodilation. In morphine tolerant and beta-endorphin tolerant rats, morphine and beta-endorphin each produced hyperthermia due to increased metabolism. Naloxone produced a dose dependent hypothermia and abstinence syndrome in morphine and beta-endorphin tolerant rats, but not in the saline group. 26 references. (Author abstract modified)

**002864** Lin, M. T.; Chern, Y. F.; Chow, C. F.; Li, Y. P. Dept. of Physiology and Biophysics, National Defense Medical Center, Taipei, Taiwan **Effects of brain serotonin alternations on hypothermia produced by chlorpromazine in rats.** Pharmacology. 18(3):128-135, 1979.

The hypothermia induced by chlorpromazine (CPZ) in male Sprague-Dawley rats was greatly enhanced by depression of functional serotonin or depletion of brain serotonin levels with p-chlorophenylalanine, 5,6-dihydroxytryptamine, or raphe lesions. Tryptophan, which depresses the firing of raphe units, and chlorimipramine, which inhibits serotonin reuptake, also greatly enhanced the CPZ-induced hypothermia. Results indicate that central serotonergic activity is involved in the modulation of CPZ-induced hypothermia. 24 references. (Author abstract modified)

**002865** Lin, M. T.; Pang, I. H.; Chern, S. I.; Chern, Y. F. Dept. of Physiology and Biophysics, National Defense Medical Center, Taipei, Taiwan **Effects of increasing serotonergic receptor activity in brain on prostaglandin E1-induced fever in rabbits.** Pharmacology. 18(4):188-194, 1979.

The effects on increasing serotonergic receptor activity or functional serotonin (5HT) in brain on fever induced by intraventricular administration of prostaglandin-E1 were examined in male New Zealand rabbits. The prostaglandin-E1-induced fever was reduced by intraventricular or i.p. administration of the 5-HT reuptake inhibitors fluoxetine and chlorimipramine with benserazide, a peripheral decarboxylase inhibitor. Results suggest that brain 5-HT plays a role in the elaboration or modulation of prostaglandin-E1-induced fever. 22 references. (Author abstract modified)

**002866** Linseman, Mary Ann. Addiction Research Foundation, Toronto, Canada M5S 2S1 **Effects of morphine on cortex, hippocampus and medial thalamus: a comparison between urethane-anaesthetized and paralyzed-awake rats.** Brain Research Bulletin. 5(2):121-125, 1980.

The effect of morphine on cortical EEG and single units of hippocampus and medial thalamus were compared in urethane anesthetized and paralyzed awake rats. In each case there is evidence of a morphine/urethane interaction. This suggests caution in the interpretation of drug studies using urethane anesthetized rats. Finally, it is reported that recovery was insignificantly longer in the urethane as compared to the paralyzed animals. 13 references. (Author abstract modified)

**002867** Lockard, Joan S.; Levy, Rene H.; DuCharme, Larry L.; Congdon, William C. Child Development and Mental Retardation Center, University of Washington, Seattle, WA 98195 **Cinromide's metabolite in monkey model: gastric administration and seizure control.** Epilepsia. 21(2):177-182, 1980.

The efficacy of Cinromide (3 bromo-N-ethylcinnamamide) in terms of clinical seizures was examined in rhesus monkeys. Cinromide's major metabolite (3-bromocinnamamide, BC) was the main focus. Eight alumina-gel monkeys were given by gastric bolus every 6 hr for 10 days (Phase I) either the solvent alone (Tween 80), Cinromide (BEC), or its synthetic metabolite (SBC). Subsequently (Phase II), four animals were given BEC or SBC by chronic gastric infusion for 20 days. In both phases Cinromide's metabolite (either via BEC or especially SBC) was effective in half of the animals in reducing seizure frequency and/or duration at plasma levels above 5mcg/ml. The data suggest that the drug's efficacy is individually specific. Another species of Cinromide metabolism, 3-bromocinnamic acid, is also discussed. 3 references. (Author abstract modified)

**002868** London, Edythe D.; Klemm, Nikolai; Coyle, Joseph T. Coyle: Dept. of Pharmacology, Johns Hopkins University School of Medicine, 725 North Wolfe St., Baltimore, MD 21205

**Phylogenetic distribution of (3H)kainic acid receptor binding sites in neuronal tissue.** Brain Research. 192(2):463-476, 1980.

The phylogenetic distribution of specific binding sites for kainic acid was determined in 14 species including vertebrates and invertebrats. The highest level of binding was observed in the frog brain, followed by spiny dogfish, goldfish, and chick brains. In most cases, specific binding to both high and low affinity sites was detected. In mammalian species, the highest level of binding was seen in the forebrain, with less in the cerebellum and least in the medulla. Binding kinetics for (3H) kainic acid were similar for frog whole brain, rat forebrain, and human parietal cortex. 36 references. (Author abstract modified)

**002869** Lukas, Scott Edward. University of Maryland Baltimore Professional Schools **Neuropharmacology of levo-alpha-acetylmethadol (LAAM): electroencephalographic and behavioral correlates. (Ph.D. dissertation).** Dissertation Abstracts International. 40(11):5226-B, 1980. Ann Arbor, Univ. Microfilms No. 8011473, 129p., 1979.

Three aspects of the pharmacodynamics of levo-alpha-acetylmethadol (LAAM), a potential alternative to methadone, (effects of acute administration of LAAM and its metabolites, degree of cross-tolerance to other narcotics during chronic LAAM administration and suppression of opiate seeking behavior during chronic LAAM administration) were investigated in rats. It is concluded that the freely moving rat bearing EEG electrodes and cannulae provide an excellent model for studying narcotic drug abuse. Quantitation of the EEG established dose response relationship for LAAM and its two metabolites as compared with morphine and methadone. LAAM's unique pharmacologic profile appears to be mediated via its metabolites. In addition, chronic administration of LAAM at doses which produce a substantial degree of cross tolerance to narcotic challenges also effectively suppresses opiate seeking behavior. (Journal abstract modified)

**002870** Lupa, Krystyna; Wojcik, Grazyna; Niechaj, Andrzej. Dept. of Human Physiology, Medical School, Dymitrowa 11, P1-20-080 Lublin, Poland **Differential depression by apomorphine of the dorsal root potentials spreading caudally and cranially in the cat spinal cord.** Naunyn-Schmiedeberg's Archives of Pharmacology. 310(1):21-24, 1979.

The effect of apomorphine on bilateral dorsal root potentials (DRPs) spreading caudally and cranially along three segments of the lower spinal cord was studied in spinal cats anesthetized with thiamylal sodium. Apomorphine in a dose of 5mg/kg i.v. depressed ipsilateral DRPs spreading caudally to 77% of their initial amplitude, and the period of depression was 50 minutes. DRPs spreading cranially were depressed to 59% of initial amplitude, and depression lasted for about 60 minutes. Contralateral DRPs spreading cranially were also more depressed than those spreading caudally. The depression of DRPs varied with apomorphine dose, but not with changes in stimulation strength. Pimozide and haloperidol blocked the apomorphine-induced depression of DRPs. It is suggested that differences in the depression of DRPs spreading caudally and cranially result from the different numbers of dopaminergic neurons terminating on interneurons transmitting depolarization cranially and caudally. 19 references. (Author abstract modified)

**002871** Luthra, Yugal K. Dept. of Biochemical Pharmacology, Mason Research Insitute, Worcester, MA 01609 **Brain biochemical alterations in neonates of dams treated orally with delta9-tetrahydrocannabinol during gestation and lactation.** In: Nahas, G., Marihuana: biological effects. Oxford, Pergamon, 1979. 777 p. (p. 531-537).

To determine brain biochemical alterations in neonates of dams treated orally with delta9-tetrahydrocannabinol (THC), brain protein and nucleic acid levels were measured in neonates treated with THC doses of 0, 1, 5, or 10mg/kg during gestation or gestation and lactation. These doses were calculated to represent human use, were nonteratogenic, and did not provoke adverse effects on the dams, as determined by reproductive data and endocrine organ and body weights. Results show that treatment during gestation with 5mg/kg induced 11% decline in protein, whereas 10mg/kg dose regimen caused approximately 13% decrease in protein, RNA, and DNA in less than 1 day old offsprings When the drug was given during gestation and lactation, the analysis of brains from 7 day old offsprings revealed 10 to 12% fall in protein and RNA concentration in the 5mg/kg group. At 10mg/kg dose, a 15% decrease occurred in protein and nucleic acid levels. Results suggest that the effect of THC on the neonate brain macromolecules are determinant factors in producing behavioral aberrations in the developing organism. 23 references. (Author abstract modified)

**002872** Lyles, Geoffrey A.; Callingham, Brian A. Dept. of Pharmacology, University of Cambridge, Hills Road, Cambridge CB2 2QD, England **Short- and long-term effects of L-DOPA treatment upon monoamine oxidase: a comparative study in several rat tissues.** European Journal of Pharmacology. 61(4):363-372, 1980.

The effects of chronic administration of L-DOPA (250mg/kg/day for up to 26 days) on the oxidative deamination of 5-hydroxytryptamine, dopamine, and benzylamine were studied in male Sprague-Dawley rat tissue homogenates. The metabolism of these amines was generally increased in the cardiovascular tissues and kidneys after L-DOPA treatment. Relatively few changes were observed in brain and liver. Possible selective influence of L-DOPA on type-A and type-B monoamine oxidase and clorgyline resistant amine oxidase activities are discussed. 27 references. (Author abstract modified)

**002873** Lyness, William H.; Mycek, Mary J. Mycek: College of Medicine and Dentistry of New Jersey, Dept. of Pharmacology, 100 Bergen St., Newark, NJ 07103 **The role of cerebral serotonin in the development of tolerance to centrally administered phenobarbital.** Brain Research. 187(2):443-456, 1980.

Depletion of serotonin with p-chlorophenylalanine, p-chloroamphetamine, or 5,7-dihydroxytryptamine did not affect the initial response to centrally injected phenobarbital in male Sprague-Dawley rats, but all three treatments significantly delayed the development of tolerance to the barbiturate. Steady-state levels of serotonin and 5-hydroxyindoleacetic acid (5-HIAA) in different brain areas were comparable in controls and tolerant rats at various stages of tolerance development. However, the temporal patterns of 5-HIAA elevation in the striatum, hypothalamus, and midbrain differed in tolerant and nontolerant rats during the phenobarbital-induced loss of righting reflex. 36 references. (Author abstract modified)

**002874** Lyness, William Harold. College of Medicine and Dentistry of New Jersey, Graduate School of Biomedical Sciences **The role of brain serotonin in barbiturate tolerance development and maintenance. (Ph.D. dissertation).** Dissertation Abstracts International. 40(9):4248-B, 1980. Ann Arbor, Univ. Microfilms No. 8006565, 208p., 1978.

The role of brain serotonin (5-HT) in barbiturate tolerance development and maintenance was investigated. Depletion of 5-HT with p-chlorophenylalanine, p-chloramphetamine or 5,7-dihydroxytryptamine did not change the naive dose response curve to i.c.v. phenobarbital, but all produced significant delays in tolerance development. The basal levels of 5-HT or the con-



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centrations of 5-hydroxyindoleacetic acid (5-HIAA) in tolerant rats are not different from controls when examined at different stages of tolerance development. Tolerant animals sacrificed after an i.c.v. phenobarbital challenge show a different pattern of 5-HIAA elevations than control rats. In vitro and in vivo data suggest three possible sites for adaptive changes in serotonergic neurons after chronic barbiturate injection: 1) regulation of tryptophan uptake; 2) presynaptic membranes; and 3) mediation of 5-HT release by nonserotonergic neurons. (Journal abstract modified)

**002875** Maggi, Adriana; U'Prichard, David C.; Enna, Salvatore J. Enna: Dept. of Neurobiology and Anatomy, University of Texas Medical School, P. O. Box 20708, Houston, TX 77025 **Differential effects of antidepressant treatment on brain monoaminergic receptors.** European Journal of Pharmacology. 61(2):91-98, 1980.

Chronic (21 day) administration of imipramine or desipramine resulted in a decrease in serotonin and beta-adrenergic receptor binding in selected brain regions of male Sprague-Dawley rats, but did not alter muscarinic cholinergic receptor binding. Receptor binding was not altered by chronic administration of the norepinephrine uptake inhibitor nisoxetine or the serotonin uptake inhibitor fluoxetine. Some antidepressants were potent alphal-receptor blocking agents in vitro, but all classical and nonclassical antidepressants tested showed weak affinity for alpha2-receptors (with the exception of mianserin, which had equal affinity for alpha1 and alpha2 receptor sites). 24 references. (Author abstract modified)

**002876** Mandl, G.; Desai, N.; Capaday, C. Aviation Medical Research Unit, Dept. of Physiology, McGill University, Montreal, Quebec, Canada **Nitrous oxide modifies visual responses in the cat retina, striate cortex and superior colliculus.** Brain Research. 193(2):401-414, 1980.

Extracellular records from single cells in cat optic tract, visual cortex, and superior colliculus showed that ventilation with a mixture of 70% nitrous oxide (N20) and 30% oxygen modified unit responses to visual stimuli. About half (57%) of the units in the optic tract were affected by N20, compared to 28% in the visual cortex and 86% in the superior collicus. The temporal distrubtion of unit firing and the degree of directional preference were altered in some cells. Responses to flashed or moving stimuli were reduced or abolished in some cells, and resting discharge rate showed sharp increases or decreases. 38 references. (Author abstract modified)

**002877** Marchais, Dominique; Bockaert, Joel. Bockaert: Laboratoire de Physiologie Cellulaire, Collegε de France, 11 Place Marcelin Berthelot, F-75231 Paris Cedex 05, France **Is there a connection between high affinity 3H-spiperone binding sites and DA-sensitive adenylate cyclase in corpus striatum?** Biochemical Pharmacology. 29(10):1331-1336, 1980.

The possibility of a connection between the high affinity 3H spiperone binding sites and the dopamine sensitive adenylate cyclase system suggested by recent studies was investigated in corpus striatum. When measured under identical conditions (membrane preparation, incubation conditions, presence of dopamine), the affinity of spiperone for its binding site was much higher than its affinity for inhibiting the dopamine sensitive adenylate cyclase. Phenoxybenzamine was found to block 3H spiperone binding irreversibly. Phenoxybenzamine completely suppressed 3H spiperone binding while the adenylate cyclase continued to be stimulated by dopamine (35% of control stimulation) and inhibited by spiperone or haloperidol. The affinities of these neuroleptics for inhibiting the dopamine sensitive adenylate cyclase were the same on control and phenoxybenzamine treated membranes. Consequently, the 3H spiperone binding site does not have to be occupied to allow inhibition of the dopamine sensitive adenylate cyclase. Guanosine triphosphate reduced the affinities of dopamine, RU 24926, and serotonin for 3H spiperone binding sites and did not affect the affinity of 2-Br-alpha-ergocriptine. Since RU 24296 and serotonin neither stimulate nor inhibit the dopamine sensitive adenylate cyclase, the effects of guanosine triphosphate on binding do not appear related to adenylate cyclase activation by agonists which is known to require guanosine triphosphate. Results suggest that the high affinity 3H spiperone binding sites are not related to the dopamine sensitive adenylate cyclase. 31 references. (Author abstract modified)

**002878** Marek, Kenneth L.; Roth, Robert H. Dept. of Pharmacology, Yale University School of Medicine, New Haven, CT 06510 **Ergot alkaloids: interaction with presynaptic dopamine receptors in the neostriatum and olfactory tubercles.** European Journal of Pharmacology. 62(2/3):137-146, 1980.

The ergot alkaloids bromocriptine, ergocornine, and lergotrile had potent agonist action at presynaptic dopamine (DA) receptors on striatal and mesolimbic nerve terminals in male Sprague-Dawley rats. These agents blocked the increase in striatal dihydroxyphenylalanine accumulation produced by gamma-butyrolactone. Pretreatment with haloperidol prevented the inhibitory effects of apomorphine and of the ergot alkaloids. However, when haloperidol was given 50 minutes after the agonists, it completely blocked the effects of apomorphine, partially blocked the effects of ergocornine and lergotrile, and failed to alter the effect of bromocriptine. 30 references. (Author abstract modified)

**002879** Mares, P.; Rokyta, R. Institute of Physiology, Czechoslovak Academy of Science, Budejovicka 1083, 142 20 Prague 4, Czechoslovakia **Motor patterns of seizures during ontogenesis in rats.** Activitas Nervosa Superior. 21(1):21, 1979.

Motor patterns of seizures elicited by metrazol, isonicotine hydrazide, and aminooxyacetic acid (AOAA) during ontogenesis in rats were investigated. Comparison of seizures elicited by metrazol, isonicotine hydrazide and AOAA demonstrates that the motor pattern of seizures in developing animals is determined by two factors: developmental stage of the CNS (especially expressed in metrazol-induced seizures) and the specificity of an epileptogenic agent. Changing sensitivity to the epileptogenic action of AOAA during ontogenesis is cited as an area for further inquiry. 3 references.

**002880** Marwaha, Jwaharlal; Palmer, Michael; Hoffer, Barry; Freedman, Robert. Dept. of Psychiatry, University of Colorado Health Sciences Center, 4200 East Ninth Avenue, Denver, CO 80262 **Phencyclidine-induced depressions of cerebellar Purkinje neurons.** Life Sciences. 26(18):1509-1515, 1980.

A dose dependent slowing of the spontaneous discharge of Sprague-Dawley rat cerebellar Purkinje neurons following local administration of phencyclidine (PCP) by pressure ejection is reported. Ketamine also depressed firing and was much less potent than PCP. Effects of both PCP and ketamine were antagonized by local or parenteral administration of antipsychotic drugs. The similarities between the electrophysiological and behavioral actions of PCP suggest that alterations in neuronal discharge may underlie its psychotomimetic properties. 16 references. (Author abstract modified)

**002881** Mathison, R. D.; Dreifuss, J. J. Dreifuss: Dept. of Physiology, University of Geneva Medical School, 1211 Geneva 4, Switzerland **Structure-activity relationships of a neurohypophysial GABA receptor.** Brain Research. 187(2):476-480, 1980.

The effects of GABA and several conformationally restricted analogues on the antidromically conducted compound action potential (CAP) in the isolated neurohypophysial/infundibular preparation of the rat were compared. Results showed that the neurohypophysial GABA receptor is selective for a structure in which the terminal and carboxyl moieties are separated by three unsubstituted methylene groups (a structure defining the GABA molecule). Shortening the carbon chain to one carbon (glycine) resulted in an increase of 25% in the amplitude of the CAP. 19 references.

**002882** Mathura, C. B.; Meier, G. W.; Himwich, W. A. Dept. of Psychiatry, Howard University College of Medicine, Washington, DC 20060 **Experimental manipulation of acetylcholine levels in developing rat brain: neurochemistry and behavior.** Psychological Reports. 45(3):811-818, 1979.

An attempt to manipulate experimentally the acetylcholine (ACh) system during rapid development of the rat brain is reported. Developmental periods of ACh manipulated were 2 to 15 days and 15 to 28 days postnatally. The findings show that the highest level of drug manipulation (0.75mg/kg physostigmine and 0.025mg/kg methscopolamine) significantly produced the highest level of ACh and the lowest activity levels of both acetylcholinesterase and choline acetylcholinesterase and choline acetyltransferase as compared to the intermediate, and control doses. This dose response relationship was obtained in the animals injected over a 15 to 28 day period during the period of maximal growth of the acetylcholine system. These statistically significant differences measured at 24 hr. after injection support the thesis that injections during the critical period of development produce longer lasting effects than if administered at other periods. Behavioral measures, GO:NO-GO discrimination avoidance tasks, were also both significantly related to the highest dose group yet were not differentiated to developmental periods of injections. 25 references. (Author abstract)

**002883** Max, Stephen R.; Knudsen, James F. Dept. of Neurology, University of Maryland, School of Medicine, Baltimore, MD 21201 **Neural and endocrine interaction in skeletal muscle.** Brain Research. 190(2):549-553, 1980.

The effects of estrogens on the neurotrophic control of muscle glucose 6-phosphate dehydrogenase (G6PD) activity, the rate limiting enzyme of the pentose phosphate pathway, in Charles River rats were examined. The extent of the increase in G6PD activity was similar in male and female rats; the rate of the increase was different. The data can be interpreted to suggest either that androgens attenuate the expression of the denervation effect on G6PD activity or that estrogens accelerate it. It is concluded that stereospecific estrogen receptors, which have been reported to be present in skeletal muscle, influence the rate of increase of G6PD activity after denervation. 15 references.

**002884** McClain, R. M.; Hoar, R. M. Hoffman-La Roche Inc., Research Division, Dept. of Toxicology, Nutley, NJ 07110 **The effect of flunitrazepam on reproduction in the rat. The use of cross-fostering in the evaluation of postnatal parameters in rat reproduction studies.** Toxicology and Applied Pharmacology. 53(1):92-100, 1980.

The effects of flunitrazepam, a benzodiazepine derivative, on reproduction in the rat were studied. Female rats treated with 25mg/kg/day flunitrazepam showed central nervous system depression, indifference during parturition, and a tendency toward cannibalization of their young. In a cross-fostering experiment, treated dams cannibalized control pups that they were nursing indicating that cannibalism was due to abnormal maternal behavior. Treated pups with control dams had a lower survival rate than control pups with control dams, suggesting that decreased viability of pups delivered from treated dams was an additional factor in neonatal loss. The survival rate of Caesarean delivered pups, however, from treated dams and fostered by control dams was not significantly different from that of control pups similarly handled. These results demonstrate that the decreased viability of pups from treated dams appears to be the result of trauma during delivery rather than a direct toxic effect of flunitrazepam on the neonate or on the fetus in utero. 13 references. (Author abstract modified)

**002885** McCulloch, James; Savaki, Helen E.; McCulloch, Mailis C.; Sokoloff, Louis. University of Glasgow, Glasgow, Scotland **Specific distribution of metabolic alterations in cerebral cortex following apomorphine administration.** Nature. 282(5736):303-305, 1979.

The specific distribution of metabolic alterations in cerebral cortex following apomorphine administration was investigated in rats, via the 2-deoxyglucose technique in conjunction with conventional neuropharmacological techniques. The sensitivity to apomorphine of glucose utilization in areas such as layer VI of the sensory motor cortex, and the prevention of the apomorphine-induced alterations in glucose utilization in all cortical areas by low doses of the dopamine antagonist, haloperidol, suggest a key involvement of dopaminergic receptors in the responses observed. The finding that the cortical involvement in the action of apomorphine extends beyond the known confines of the mesocortical dopaminergic system suggests a need for reappraisal of the mechanisms and foci of action underlying the behavioral effects of antipsychotic and other drugs used to manipulate dopaminergic systems in the CNS. 11 references.

**002886** McGeer, P. L.; Jakubovic, A. Kinsmen Laboratory of Neurological Research, Dept. of Psychiatry, University of British Columbia, Vancouver, B.C., V6T 1W5, Canada **Ultrastructural and biochemical changes in CNS induced by marihuana.** In: Nahas, G., Marihuana: biological effects. Oxford, Pergamon, 1979. 777 p. (p. 519-530).

The effect of delta9-tetrahydrocannabinol (THC) on some metabolic processes and cell structures in rat brain were studied in vitro and in vivo. The intracellular distribution and binding of labeled THC in brain tissue was also determined. The following results were observed: 1) the incorporation of radioactive precursors into protein and nucleic acid of rat brain cortical slices was significantly inhibited by THC; 2) acute administration of THC and other cannabinoids initiated morphological changes, viz. a reduction in the number of nuclear membrane attached ribosomes in rat brain; 3) following the administration of radioactive THC to lactating rats, THC and its metabolites were identified in the organs of sucking infants; and 4) intracellular distribution studies with labeled THC show highly preferential binding to particulate fractions in the brain cells, mainly the crude mitochondrial fraction. Findings suggest the subcellular distribution and binding of the cannabinoids and their effects on synthesis processes plays important roles in their physiological and pharmacological effects. 25 references. (Author abstract modified)

**002887** McMillen, Brian A. Dept. of Pharmacology, University of Texas Health Science Center, Dallas, TX 75235 **On the mechanism of morphine action on rat striatal dopamine metabolism.** Biochemical Pharmacology. 29(10):1432-1435, 1980.

The mechanism of morphone action on rat striatal dopamine metabolism was investigated via administration of the potent CNS stimulant amfonelic acid (AFA), gamma-butyrolactone, haloperidol, morphine sulfate, and naloxone HCl (in various combinations), and assessment of dopamine metabolism. AFA was used to differentiate possible mechanisms of morphine-in-

duced increased dopamine metabolism. That AFA is dependent upon impulse flow to enhance dopamine release and metabolism is supported by the haloperidol dose/response curve. The combination of AFA with a dose of haloperidol insufficient to inhibit the stimulant effects of AFA results in DOPAC concentrations lower than with haloperidol alone, but greater than control. When sufficient haloperidol is used to inhibit AFA-induced behavioral stimulation and reduction of impulse flow, a marked synergism between these two drugs on dopamine metabolism is observed. However, AFA exhibits only an additive effect on dopamine metabolism when combined with morphine. The lack of antagonism of morphine by AFA suggests that the increased dopamine metabolism caused by morphine is not mediated by the sequence of decreased release leading to loss of dopamine at the presynaptic autoreceptor causing enhanced tyrosine hydroxylase activity. It is hypothesized that the two effects of morphine, enhanced dopamine metabolism and impulse flow, reflect activation of opiate receptors at two unrelated sites, and the amount of dopamine released will reflect the sum of these two phenomena. 20 references.

**002888** McMillen, Brian A.; Shore, Parkhurst A. Dept. of Pharmacology, University of Texas Health Science Center, 5323 Harry Hines Blvd., Dallas, TX 75235 **Species-dependent responsiveness to nonamphetamine central stimulants: relationship between uptake and release of brain dopamine.** Pharmacology. 19(5):261-266, 1979.

Amfonelic acid (AFA), which has potent stimulant effects in rats, had little or no stimulatory effect in rabbits. However, AFA inhibited the accumulation of dopamine (DA) by both rat and rabbit striatal synaptosomes, suggesting that DA uptake inhibition does not per se cause stimulation. AFA raised DA metabolites in rat striatum, but had no effect in the rabbit. AFA also potentiated the ability of haloperidol to increase brain DA metabolism in rat but not in rabbit. A mechanism to account for these species differences is proposed. 14 references. (Author abstract modified)

**002889** McMillen, Brian A.; Warnack, Worthy; German, Dwight C.; Shore, Parkhurst A. Dept. of Pharmacology, University of Texas Health Science Center, Dallas, TX 75235 **Effects of chronic desipramine treatment on rat brain noradrenergic responses to alpha-adrenergic drugs.** European Journal of Pharmacology. 61(3):239-246, 1980.

In female Sprague-Dawley rats treated chronically with desipramine (5.0mg/kg i.p., twice each day), brain norepinephrine (NE) levels were decreased after 7 days and brain NE metabolism was enhanced after 12 dyas. Neuronal firing in the locus coeruleus of rats treated with desipramine for 1 week was lower than that in controls, but higher than that in rats treated acutely with desipramine. Brain NE metabolism in control rats was decreased equally by 25 and 250mcg/kg doses of clonidine, but only the higher dose decreased NE metabolism in rats given desipramine for 12 days. Results suggest that presynaptic alpha-adrenoceptors become subsensitive during long-term desipramine treatment, permitting recovery of noradrenergic impulse flow in the presence of NE uptake inhibition. 28 references. (Author abstract modified)

**002890** Meldrum, B. S.; Menini, C.; Naquet, R.; Laurent, H.; Stutzmann, J. M. Dept. of Neurology, Institute of Psychiatry, London SE5 8AF, England **Proconvulsant, convulsant and other actions of the D- and L-stereoisomers of allylglycine in the photosensitive baboon, Papio papio.** Electroencephalography and Clinical Neurophysiology. 47(4):383-395, 1979.

The effects of intravenous or intracerebroventricular injection of the stereoisomers, and the racemic mixture, of allylglycine (2-amino-bent-4-enoic acid) were studied in eight baboons, Papio papio, with photosensitive epilepsy. Enhancement of the natural syndrome of photosensitive epilepsy was seen 1 to 12 hr (maximally at 3 to 8 hr) after 100mg/kg L-allylglycine i.v., or 200mg/kg D,L-allylglycine i.v. Enhancement, but with slower onset and to a lesser and more variable extent, was seen after 500 to 750mg/kg D-allylglycine i.v. Brief focal or generalized seizures occurred in the absence of intermittent photic stimuli after L-allylglycine, 150 to 200mg/kg i.v. Intracerebroventricular L-allylglycine, D-allylglycine, or D,L-allylglycine, 100mg in 1ml saline, did not modify the natural syndrome of photosensitive epilepsy; however D-allylglycine and D,L-allylglycine after 1 to 2 hr gave rise to a syndrome with vomiting, sustained vertical nystagmus, and intermittent extensor spasms. Results are interpreted in terms of regional differences in the metabolism of the two isomers to active compounds that can inhibit glutamic acid decarboxylase. D-allylglycine is active only at the brain stem and cerebellum because D-amino acid oxidase is largely confined to these areas. 34 references. (Author abstract modified)

**002891** Meltzer, H. Y.; Fessler, R. G.; Simonovic, M.; Doherty, J.; Fang, V. S. Dept. of Psychiatry, University of Chicago Pritkzer School of Medicine, Chicago, IL **Effect of d- and l-amphetamine on rat plasma prolactin levels.** Psychopharmacology. 61(1):63-69, 1979.

Prolactin secretion was utilized to investigate several aspects of the action of amphetamine and to understand the physiology of the tuberoinfundibular neurons in relation to prolactin secretion. Although d-amphetamine and l-amphetamine had no effect on plasma prolactin levels in untreated male rats, both d-amphetamine and l-amphetamine reversed the increase in plasma prolactin levels produced by reserpine and 5-hydroxytryptophan (5-HTP). Only d-amphetamine significantly reversed the effect of alpha-methylparatyrosine (AMPT) on plasma prolactin levels. The effect of d-amphetamine on the increase in plasma prolactin levels produced by reserpine, 5-HTP, or AMPT was always greater than that of the l-isomer, suggesting that the d-isomer has a more profound effect than l-amphetamine. 59 references. (Author abstract modified)

**002892** Miglecz, Erzsebet; Szekely, J. I.; Dunai-Kovacs, Zsuzsa. Dept. of Pharmacology, Research Institute for Pharmaceutical, Chemistry, H-1325 Budapest, PO Box 82, Hungary **Comparison of tolerance development and dependence capacities of morphine, beta-endorphin, and (D-MET2, PRO5)-enkephalinamide.** Psychopharmacology. 62(1):29-34, 1979.

The tolerance development capacities of beta-endorphin (D-Met2,Pro5)-enkephalinamide and morphine were compared in rats, and the dependence capacity of morphine was compared with that of the enkephalin analogue in mice. Tolerance to the analgesic effect as measured by the tail flick test developed somewhat more rapidly in the Met-enkephalin group than in the others. A similar relationship was found for the dependence capacity. Considering that the enkephalin analogue displayed the strongest analgesic activity, the well known correlation between antinociceptive and tolerance development/dependence capacities of opiates seems to be valid for opioid peptides as well. 26 references. (Author abstract)

**002893** Miller, Harold H.; Shore, Parkhurst A.; Clarke, David E. Clarke: Dept. of Pharmacology, University of Houston, TX 77004 **In vivo monoamine oxidase inhibition by d-amphetamine.** Biochemical Pharmacology. 29(10):1347-1354, 1980.

The hypothesized in vivo monoamine oxidase (MAO) inhibition by D-amphetamine was investigated in rats. D-amphetamine was more effective than l-amphetamine at decreasing

striatal 3, 3, 4-dihydroxyphenylacetic acid (DOPAC), but assays of striatal MAO activity following administration of amphetamine in vivo failed to show MAO inhibition. In other experiments, rats were treated with d-amphetamine (zero time) followed by phenelzine (1 hour), an irreversible MAO inhibitor, and were killed at 25 hours. MAO activity was determined in vitro for the striatum and the rest of the brain using serotonin (MAO-A) and phenylethylamine (MAO-B) as substrates. d-amphetamine provided significant protection against MAO-A inhibition by phenelzine, whereas l-amphetamine and cocaine (used instead of amphetamine) were without effect. D-amphetamine failed to protect against MAO-B inhibition by phenelzine. Thus, D-amphetamine appears to inhibit reversibly MAO type-A in vivo. However, using the same protection protocol, D-amphetamine failed to oppose phenelzine-induced lowering of striatal DOPAC. Experiments were undertaken to determine whether the protective effect of d-amphetamine on MAO type- A would influence striatal dopamine depletion by Ro4-1284, a rapidly-acting reserpine-like agent. Ro4-1284-induced depletion of dopamine was inhibited by phenelzine. Prior treatment with d-amphetamine reduced significantly the protective effect of phenelzine, suggesting reversible, intraneuronal MAO inhibition by d-amphetamine in vivo. The possible neuronal mechanisms for these events are discussed. 41 references. (Author abstract modified)

**002894** Modak, A. T.; Stavinoha, W. B.; Hagino, N. Dept. of Pharmacology, University of Texas Health Science Center, 7703 Floyd Curl Drive, San Antonio, TX 78284 **Involvement of the cholinergic system in the precocious puberty caused by estradiol in immature female rats.** Archives Internationales de Pharmacodynamie et de Therapie. 241(2):344-350, 1979.

Subcutaneous administration of 0.5mcg estradiol benzoate to sexually immature female Sprague-Dawley rats caused precocious ovulation and decreased acetylcholine (ACh) content in the hypothalamus and amygdala. A higher dose (2mcg) did not stimulate ovulation, but did further decrease the ACh content in hypothalamus and amygdala. The steady-state levels of ACh in the hippocampus and striatum were not changed by either dose of estradiol. Results suggest a relationship between ovulation and the decrease in the steady-state level of ACh in the hypothalamus and amygdala of the sexually immature rat after estradiol treatment. 35 references. (Author abstract modified)

**002895** Morgan, William W.; Kamp, Cylia W. Dept. of Anatomy, University of Texas Health Science Center, 7703 Floyd Curl Drive, San Antonio, TX 78284 **A GABAergic influence on the light-induced increase in dopamine turnover in the dark-adapted rat retina in vivo.** Journal of Neurochemistry. 34(5):1082-1086, 1980.

Pharmacologic manipulation of the GABA system was found to modify the light-induced change in dopamine (DA) turnover. The decline in DA content following inhibition of tyrosine hydroxylase by alpha-methyl-p-tyrosine (alpha MPT) was used to estimate DA turnover. The decline in DA content in retinas of the alpha MPT treated rats was significantly enhanced by light exposure for 30 to 60 min. Two doses of the potent GABA agonist muscimol significantly inhibited the light-induced increase in DA turnover. This action was selective for GABA because the GABA antagonist picrotoxinin reversed the muscimol mediated blockade of the light-induced stimulation. In fact, DA turnover in the presence of light, muscimol, and picrotoxinin was not different from DA turnover in the presence of light alone. These data suggest that there is either a direct or indirect GABAergic input to the DA system of the rat retina. 20 references. (Author abstract modified)

**002896** Mori, Junko; Fukuda, Takeo. Dept. of Physiology, National Defense Medical College, Tokorozawa, Saitama 359, Japan **Effects of pentylenetetrazol, pentobarbital, and lidocaine on pallidal unit activities in rats.** Japanese Journal of Pharmacology. 29(3):405-411, 1979.

Pallidal unit activities were recorded extracellularly following injection of pentylenetetrazol, lidocaine, and pentobarbital in Wistar rats. Pentylenetetrazol (20mg/kg i.v.) markedly increased burst discharges, and the bursts tended to synchronize with repetitive spikes in the electrocorticogram. Lidocaine (5mg/kg i.v.) facilitated the pentylenetetrazol enhanced bursts in about 70% of neurons, whereas pentobarbital reduced these bursts in 80%; both drugs reduced the firing rate. Facilitation of burst discharges was also seen after high doses of lidocaine alone. 15 references. (Author abstract modified)

**002897** Morley, J. E.; Yamada, T.; Walsh, J. H.; Lamers, C. B.; Wong, H. Neuroendocrine Research Laboratory, Minneapolis VA Hospital, Minneapolis, MN 55417 **Morphine addiction and withdrawal alters brain peptide concentrations.** Life Sciences. 26(26):2239-2244, 1980.

Profound alterations in the concentrations of a variety of brain peptides during morphine addiction and withdrawal in rats are described. Somatostatin, cholecystokinin, neurotensin, and substance-P concentrations increased during morphine addiction. Naloxone-induced withdrawal decreased brain concentrations of TRH, somatostatin, neurotensin, and substance-P. Naloxone alone decreased thalamic substance-P and neurotensin concentrations. Vasoactive intestinal peptide concentrations were unaltered by any of the treatments. The fall in the tissue concentration of somatostatin during a naloxone-induced withdrawal correlated well with the fall in the circulating growth hormone, suggesting that this could be secondary to somatostatin release. These data support the hypothesis that brain peptides, acting locally in the brain as neuromodulators, play an important role in the genesis of the syndromes of morphine addiction and withdrawal. 19 references. (Author abstract modified)

**002898** Muraki, T.; Tokunaga, Y.; Nakadate, T.; Kato, R. Dept. of Pharmacology, School of Medicine, Keio University, 35 Shinanomachi, Shinjuku-ku, Tokyo 160, Japan **Inhibition by cholinergic agonists of the prolactin release induced by morphine.** Naunyn-Schmiedeberg's Archives of Pharmacology. 308(3):249-254, 1979.

The cholinergic agonists pilocarpine, physostigmine, and nicotine inhibited the prolactin release induced by morphine in male Wistar rats in vivo. Pilocarpine also inhibited the release of prolactin induced by beta-endorphin or metoclopramide, without affecting basal or haloperidol stimulated serum prolactin levels. The inhibitory effect of pilocarpine on the morphine stimulated release of prolactin was antagonized by concurrent administration of atropine, but not by atropine methylnitrate or mecamylamine; inhibition by nicotine was antagonized by mecamylamine but not by atropine. The stimulation of prolactin release by morphine and its reversal by pilocarpine were observed even after administration of haloperidol or alpha-methyltyrosine. Results suggest that the central cholinergic system exerts an inhibitory influence on the prolactin release induced by morphine or beta-endorphin and that this cholinergic inhibition is not mediated via catecholaminergic neurons. 32 references. (Author abstract modified)

**002899** Myslobodsky, Michael S.; Valenstein, Elliot S. Psychobiology Research Unit, Dept. of Psychology, Tel-Aviv University, Tel-Aviv, Israel **Amygdaloid kindling and the GABA system.** Epilepsia. 21(2):163-175, 1980.

The effect of increased GABA levels on fully kindled amygdala seizures was investigated in rats. The newly synthesized GABA transaminase inhibitor, gamma-acetylenic GABA (GAG) administered on 4 consecutive days was found to either significantly reduce, or eliminate entirely the behavioral seizures normally produced by amygdala stimulation. The effect was seen after the first injection of GAG. Behavior seizures reappeared 2 to 3 days after termination of GAG treatment. The duration of electrographic seizures was either unchanged or greater on the first day of GAG treatment, but was briefer on subsequent days. The duration of afterdischarges returned to normal levels, one to two days earlier than the behavioral seizures after the termination of GAG. Picrotoxin did not antagonize either electrographic or behavioral effects of inhibition produced with GAG. Electrical stimulation of amygdala delivered during the initial sedation stage induced by picrotoxin resulted in further regression of kindled seizures in the majority of animals. Although in doses employed, GAG alleviates amygdaloid kindled seizures its use requires caution in view of its ability to reduce arousal level. 52 references. (Author abstract)

**002900** Naber, Dieter; Wirz-Justice, Anna; Kafka, Marian S.; Wehr, Thomas A. Biological Psychiatric Branch, NIMH, Bethesda, MD 20205 **Dopamine receptor binding in rat striatum: ultradian rhythm and its modification by chronic imipramine.** Psychopharmacology. 68(1):1-5, 1980

The specific binding of 3H-spiroperidol was measured at 4 hour intervals over a 24 hour period in the striatum of male Sprague-Dawley rats housed under a controlled 12 hour light/12 hour dark cycle. A significant ultradian rhythm with peaks at 2 a.m. and 2 p.m. was observed. Chronic treatment with imipramine delayed both peaks by 4 hours and decreased the amplitude of the ultradian rhythm and the 24 hour mean of binding. Scatchard analyses indicated that changes in binding were due to changes in the number of binding sites rather than to changes in binding affinity. Results are discussed in relation to the mode of action of psychoactive drugs and to postulated changes in dopamine receptor sensitivity in neurological and psychiatric disorders. 44 references. (Author abstract modified)

**002901** Nagasaki, Hiroaki; Kitahama, Kunio; Valatx, Jean-Louis; Jouvet, Michel. Kitahama: Dept. de Medecine Experimentale, Faculte de Medecine, Universite Claude Bernard, 8 Avenue Rockefeller, F-69373 Lyon, France **Sleep-promoting effect of the sleep-promoting substance (SPS) and delta sleep-inducing peptide (DSIP) in the mouse.** Brain Research 192(1):276-280, 1980.

To further examine the sleep enhancing properties of both a brain extract from sleep-deprived rats and delta-sleep-inducing peptide (DSIP), the dose/response effects in mice of the partially purified brain stem extract, sleep promoting factor (SPS), and DSIP were compared. The dose dependent alterations of slow wave sleep (SWS) and paradoxical sleep (PS) provoked by the injection of SPS before the beginning of the dark period are described. SPS induced an SWS increase for 12 consecutive hours, with a retarded PS increase in C57BL/6 mice when injected i.p. at 19.00 hours. 11 references.

**002902** Nagayama, H.; Takagi, A.; Sakuri, Y.; Yoshimoto, S.; Nishiwaki, K.; Takahashi, R. Department of Neuropsychiatry, Nagaski University School of Medicine, Nagaski 852, Japan **Chronopharmacological study of neuroleptics: III. Circadian rhythm of brain susceptibility to haloperidol.** Psychopharmacology. 63(2):131-135, 1979.

The circadian fluctuation of the sedative effect of haloperidol was studied. Haloperidol of various doses was administered at various times during the day to rats which had been housed with strictly controlled lighting schedule and room temperature. It was shown that the sedative effect of haloperidol was significantly affected by the time of day of administration, and that the pattern changed with different doses of the drug. Time course changes in plasma and brain concentrations of the drug were measured. No significant difference in the concentrations was observed among the different times of administration. It was thus suggested that the circadian fluctuation of sedative effect of haloperidol might be due to the circadian rhythm of brain susceptibility to the drug. 21 references. (Author abstract modified)

**002903** Nagy, Ivan; Valdenegro, Carlos A.; Login, Ivan S.; MacLeod, Robert M. Department of Internal Medicine, University of Virginia School of Medicine, Charlottesville, VA 22908 **Anterior pituitary enzyme activities and prolactin secretion in male rats treated with psychotropic drugs.** Proceedings of the Society for Experimental Biology and Medicine. 162(1):191-193, 1979.

The effect of using catecholamine antagonists to manipulate prolactin release upon pituitary hexosemonphosphate shunt and glycolytic, oxidative, and lysosomal enzyme activities was investigated in rats. The injection of psychotropic drugs increased serum prolactin levels and did not significantly change anterior pituitary weight. The results suggest that estrogen and neuroleptics stimulate prolactin synthesis and that prolactin and enzyme syntheses have different gene loci in the lactotrophs. It is concluded that psychotropic dopamine antagonists primarily stimulate prolactin relaease and that their subchronic administration does not influence water-soluble protein concentration, the hexosemonophosphate shunt, or anerobic glycolytic, oxidative, and lysosomal activity of the lactotrophs. 13 references.

**002904** Nagy, J. I.; Vincent, S. R.; Staines, Wm. A.; Fibiger, H. C.; Reisine, T. D.; Yamamura, H. I. Division of Neurological Sciences, Dept. of Psychiatry, University of British Columbia, Vancouver, British Columbia V6T 1W5, Canada **Neurotoxic action of capsaicin on spinal substance P neurons.** Brain Research. 186(2):435-444, 1980.

The effects of neonatal injections of capsaicin were examined in male Wistar rats. Degeneration and glial engulfment of boutons and unmyelinated axons were observed in the dorsal horn 2 and 6 hours after subcutaneous capsaicin injections in neonatal rats. In animals sacrificed 12 weeks after the injections, no changes in glutamic acid decarboxylase or choline acetyltransferase were seen in the dorsal horn. Substance-P levels in the striatum, hypothalamus, and substratia nigra were not altered, but the substance-P content of the dorsal horn was reduced by half. The density of (3H)naloxone binding sites in the dorsal horn was significantly reduced, but their affinity was not affected. Capsaicin treated animals showed significantly increased latencies to respond to a noxious thermal stimulus in the tail flick and hotplate tests. The use of neonatal capsaicin treatment as a selective neurotoxin for the elucidation of spinal mechanisms of pain is discussed. 42 references. (Author abstract modified)

**002905** Nance, Dwight M.; Coy, David H.; Kastin, Abba J. Dept. of Anatomy, College of Medicine, University of South Florida, Tampa, FL 33612 **Experiments with a reported anorexigenic tripeptide: pyro-Glu-His-Gly-OH.** Pharmacology Biochemistry and Behavior. 11(6):733-735, 1979.

A newly described tripeptide, pyro-Glu-His-Gly-OH, which was reported to produce profound and long-term anorexia and weight loss in female mice, was initially tested in female rats. After total doses of either 8, 16, or 32mcg s.c. of the peptide, administered across an 8 day interval, there was no detectable effect on food intake, bodyweight, or estrous cycles of female

rats. In a second study, total doses of 3.4 and 6.8mcg injected in mice across a 20 day period had no effect on the food intake or bodyweight of Sprague-Dawley albino female mice. Thus, the anorexigenic potency of pyro-Glu-His-Gly-OH has yet to be established. 3 references. (Author abstract modified)

**002906** Negro-Vilar, A.; Vijayanm, E.; McCann, S. M. Dept. of Physiology, University of Texas Health Science Center, 5323 Harry Hines Blvd., Dallas, TX 75235 **The effect of intraventricular gamma aminobutyric acid (GABA) on hypothalamic catecholamines and LHRH and on pituitary hormone release.** Brain Research Bulletin. 5(3):239-244, 1980.

Intraventricular injection of GABA altered pituitary hormone release as well as release of dopamine (DA) and norepinephrine (NE) from terminals in the Sprague-Dawley rat median eminence (ME). A low dose (0.1mcMol) of GABA induced a decline in serum prolactin, but a larger (4mcMol) dose induced an increase in prolactin levels. Serum luteinizing hormone levels were increased only by the larger dose of GABA and were associated with increased luteinizing hormone releasing hormone levels in the suprachiasmatic/medial preoptic area. GABA induced marked increases in DA levels in the ME and anterior pituitary and elevated NE levels in the ME. 18 references. (Author abstract modified)

**002907** Nelson, D. L.; Herbert, A.; Pichat, L.; Glowinski, J.; Hamon, M. Hamon: Groupe NB-INSERM U 114, College de France, 11, place Marcelin Berthelot, F-75231 Paris Cedex 05, France **In vitro and in vivo disposition of 3H-methiothepin in brain tissues: relationship to the effects of acute treatment with methiothepin on central serotoninergic receptors.** Naunyn-Schmiedeberg's Archives of Pharmacology. 310(1):25-33, 1979.

A significant increase in the number of specific binding sites for tritiated 5-hydroxytryptamine (5-HT) was observed in the forebrain, particularly the hippocampus, within 2 days of i.p. injection of 20mg/kg methiothepin in male Sprague-Dawley rats. Kinetic analysis of the disposition of 3H-methiothepin in brain showed that the drug remained firmly bound to membranes for at least 10 to 12 hours after peripheral administration. This long-term occupancy of 5-HT receptors could explain the observed increase in the number of 3H-5-HT binding sites. Additional studies showed that 3H-methiothepin cannot be used as a specific ligand for 5-HT receptors in brain, since it has a high level of nonspecific binding. 34 references. (Author abstract modified)

**002908** Nestoros, J. N.; Nistri, A. Dept. of Anaesthesia Research, McGill University, Montreal, PQ, Canada H3G 1Y6 **Effects of microiontophoretically applied flurazepam on responses of cerebral cortical neurons to putative neurotransmitters.** Canadian Journal of Physiology and Pharmacology. 57(11):1324-1329, 1979.

The effects of microiontophoretically applied flurazepam on spike activity of single cerebral neurons and its interactions with several excitatory and inhibitory putative neurotransmitters were examined in the cat. Large doses (5 to 30nA, 0.1M solution or 20 to 50nA, 20mM in 0.16M NaCl) reduced the excitation produced by glutamate, aspartate, and homocysteate, but antagonism of acetylcholine evoked excitation required large flurazepam doses (up to 30nA, 0.1M solution). Even lower doses of flurazepam (less than 10nA, 20mM in 0.16M NaCl) enhanced the inhibitory effect of GABA but antagonized that of 5-hydroxytryptamine, and had no effect on dopamine-induced inhibition of firing. Only GABA evoked inhibitions were significantly potentiated by flurazepam. Results demonstrate the multiple possible interactions between a benzodiazepine and different putative neurotransmitters in the mammalian cerebral cortex. 23 references. (Author abstract modified)

**002909** Nicklas, William J.; Krespan, Barbara; Berl, Soll. Dept. of Neurology, Mount Sinai School of Medicine, Fifth Avenue & 100th St., New York, NY 10029 **Effect of kainate on ATP levels and glutamate metabolism in cerebellar slices.** European Journal of Pharmacology. 62(2/3):209-213, 1980.

Rat cerebellar slices incubated in the presence of 0.1 to 1mM kainic acid (KA) showed a significant decrease in tissue contents of ATP, glutamate, aspartate, and glutamine. The levels of glutamate and aspartate, but not glutamine, rose concomitantly in the incubation medium. Results are consistent with a multiaction mechanism for the neurotoxicity of KA. 10 references. (Author abstract modified)

**002910** Nicoll, R. A.; Wojtowicz, J. M. Dept. of Pharmacology, University of California, San Francisco, CA 94143 **The effects of pentobarbital and related compounds on frog motoneurons.** Brain Research. 191(1):225-237, 1980.

The effect of pentobarbital (PB) and related compounds on frog motoneurons was examined with sucrose gap recording from the ventral roots. PB depressed the action of glutamate, selectively enhanced the action of GABA, and elicited a GABA mimetic hyperpolarization. PB also reversed the noncompetitive picrotoxin antagonism of GABA and the competitive strychnine antagonism of beta-alanine, but not the competitive bicuculline methiodide antagonism of GABA. Phenobarbital shared all the properties of PB but was much less potent. Phenytoin showed only a weak depressant effect on glutamate responses. Chlordiazepoxide selectively enhanced GABA responses, but was devoid of other actions of PB. Chloralose shared all the actions of PB. 30 references. (Author abstract modified)

**002911** Novakova, V.; Albrecht, I.; Linhart, J. Institute of Physiology, Czechoslovak Academy of Sciences, Prague, Czechoslovakia **Total RNA content and blood flow in rat brain after RNA administration.** Activitas Nervosa Superior. 21(2):90-96, 1979.

The changes in blood flow through selected brain structures and the changes in the total RNA content of cells of these structures were examined after a single administration of yeast RNA to 6-month-old male rats. The total content of ribosomal RNA in cells of the limbic system (septum, hippocampus, hypothalamus) increased 48 hours after the administration of 100mg i.p. yeast RNA, dropped after 7 days in septum. In cells of the limbic system as a whole, there was a higher total RNA content in experimental rats. No changes were observed in the cells of parietal brain cortex. Blood flow increased in limbic structures 21 and 30 days after RNA administration and in septum and in hippocampus 90 days after application. No changes were observed in parietal brain cortex, bulbi olfactorii, cerebellum, and brainstem. Histochemical changes correlated positively with blood flow changes in the limbic system 14, 21, 30, and 90 days after RNA application. The body weight of experimental rats did not differ from that of control animals. The changes in hemodynamic parameters were transient and were demonstrated as fluctuations in heartrate, cardiac output, and peripheral resistance. No changes in blood pressure were observed. 16 references. (Author abstract modified)

**002912** Obata, Kunihiko; Oide, Momoko. Dept. of Pharmacology, Gunma University School of Medicine, 3-39-22 Showa-machi, Maebashi 371, Japan **Development of acetylcholine sensitivity of embryonic chick atria in culture.** Developmental Neuroscience. 3(1):28-38, 1980.

Atria were isolated from chick embryos of 4 to 12 days incubation and maintained up to 9 days in culture to examine change in their sensitivity to acetylcholine (ACh). Beating of atria from 4 day embryos was not affected by ACh at the start but was in-

hibited after a few days of culture. Atria from old embryos which had been sensitive to ACh remained so in culture. Desensitization to ACh was marked in short term culture of 4 day embryonic atria. Sera and embryo extracts facilitated the appearance of ACh sensitivity. Binding of quinuclidinyl benzilate was observed in ACh insensitive atria. It is reported that cyclohexidmide, puromycin, and actinomycin-D prevented the appearance and maintenance of ACh sensitivity in culture, leaving the heartbeat unaffected. 24 references. (Author abstract)

**002913** Oberlander, Claude; Dumont, Claude; Boissier, Jacques R. Centre de Recherches Roussel-Uclaf, 93230 Romainville, France **Time course of apomorphine-induced circling behaviour after striatal dopamine receptor denervation.** European Journal of Pharmacology. 62(1):107-110, 1980.

The curve describing the time course of apomorphine-induced circling behavior in male Sprague-Dawley rats with a 6-hydroxydopamine lesion of the nigrostriatal dopamine pathway was studied with a microcomputerized rotometer. The contralateral circling response was a single bell shaped curve for up to 2 weeks after lesioning, but gradually became a double peaked curve after 4 to 5 months. At this point, the bell shaped curve could be restored by pretreatment with haloperidol. 8 references. (Author abstract modified)

**002914** Ohmiya, Yoshio; Mehendale, Harihara M. Akita University School of Medicine, Akita, Japan **N-oxidation of imipramine by isolated perfused rat and rabbit lung.** Life Sciences. 26(17):1411-1421, 1980.

Pulmonary uptake and metabolism of imipramine (IMP) was investigated in isolated perfused rat (IPrL) and rabbit (IPRL) lung preparations. Perfusate containing radio labelled IMP was recirculated through the pulmonary artery in artificially ventilated lungs. The radioactivity in the perfusate declined rapidly and about 80% of the dose was taken up by the lungs within 10 minutes in both IPrL and IPRL preparations. A steady-state was apparently reached thereafter in the IPRL, while a portion of the radiolabel effluxed into the perfusate of the IPrLs, thus reducing the net lung content to 54% of added IMP by 60 minutes. After 60 minutes perfusion, metabolites of IMP accounted for the major radioactivity (80%) in the perfusate, while the lung contained mainly (83%) the unchanged parent compound. The principal metabolite was identified as IMP-N-oxide (IMP-NO) which was found in the perfusate after 5 minutes of perfusion. Only 3% of the added IMP was metabolized by IPRL in 60 minutes. SKF-525A, an inhibitor of cytochrome P-450 mediated monooxygenase system, did not inhibit but enhanced the metabolism of IMP by IPrL to IMP-NO. IMP was principally metabolized to IMP-NO by incubations of 9,000g supernatant fractions of rat lungs to a significantly higher extent than similar rabbit lung preparations. Including SKF-525A significantly accelerated the metabolism of IMP to IMP-NO in accordance with the perfusion experiments. These results suggest that in contradiction to published reports, IMP is appreciably metabolized by the rat lung via N-oxidation by noncytochrome P-450 pathway and the metabolite formed in the lung is released into the circulation indicating its low affinity for the lung tissue. 21 references. (Author abstract)

**002915** Okada, Yasuhiro; Kuroda, Yoichiro. Dept. of Neurochemistry, Tokyo Metropolitan Institute for Neurosciences, 2-6 Musashidai, Fuchu-shi, Tokyo, 183, Japan **Inhibitory action of adenosine and adenosine analogs on neurotransmission in the olfactory cortex slice of guinea pig -- structure-activity relationships.** European Journal of Pharmacology. 61(2):137-146, 1980.

Adenosine and adenine nucleotides depressed the amplitude of the postsynaptic potential (PSP) in guinea-pig olfactory cortex slices, without altering the presynaptic fiber potential. Other purine and pyrimidine derivatives had no inhibitory effect. Theopylline reversed and prevented the inhibition produced by adenosine and adenine nucleotides. A study of structure/activity relationships indicated the 6-aminopurine riboside (adenosine radical) was essential for inhibitory action on the PSP. Among adenosine analogs, the presence of at least one hydrogen atom in the amino group at the 6-position of the purine and the presence of an 0H group at the 2'-position of the ribose were essential for inhibitory activity. 28 references. (Author abstract modified)

**002916** Olesen, Ole Vendelin; Thomsen, Klaus. Psychopharmacology Research Unit, Aarhus University Institute of Psychiatry, Psychiatric Hospital, DK-8240 Risskov, Denmark **Potassium prevention of lithium-induced loss of water and sodium in rats.** Toxicology and Applied Pharmacology. 51(3):497-502, 1979.

Lithium treated rats with and without additional potassium in the food were subjected to withdrawal of water and 0.46 M NaCl solution to assess the ability of potassium to prevent lithium induced loss of water and sodium. In the course of 2 weeks the water and sodium intakes increased in all groups but they increased significantly less in the rats given potassium than in those given no extra potassium. During 6 hours of fluid deprivation the rats given extra potassium showed significantly less urine production, weight loss, and increase in serum sodium concentration. When access to NaCl solution was withdrawn the animals not given extra potassium developed lithium intoxication characterized by weight loss, decreased intake of water and food, lowered serum sodium concentration, and increased serum lithium concentration. In none of the experiments was there any difference between rats given potasssium chloride and rats given potassium phosphate. The data indicate that a high potassium content in the food prevents lithium-induced renal inability to retain water and sodium. 7 references. (Author abstract modified)

**002917** Olpe, H.-R.; Schellenberg, A. Biology Research Laboratory, Pharmaceuticals Division, Ciba-Geigy Ltd., Basel, Switzerland **Reduced sensitivity of neurons to noradrenaline after chronic treatment with antidepressant drugs.** European Journal of Pharmacology. 63(1):7-13, 1980.

The sensitivity of cingulate cortical neurons to microiontophoretically applied noradrenaline (NE) and GABA was tested in rats treated chronically with antidepressant drugs or the tricyclic antiepileptic carbamazepine. The sensitivity of cortical cells to NE was significantly reduced by chronic treatment with desipramine, clomipramine, maprotiline, or tranylcypromine, but not by chronic treatment with carbamazepine. The sensitivity of cingulate neurons to GABA was not altered by chronic treatment with these drugs. 8 references. (Author abstract modified)

**002918** Osborne, N. N.; Neuhoff, V. Max-Planck Institut fur experimentelle Medizin, Forschungsstelle Neurochemie Hermann-Rein-Str. 3, D-3400 Gottingen, Germany **Are there opiate receptors in the invertebrates?** Journal of Pharmacy and Pharmacology. 31(7):481, 1979.

Following removal of their shells, Helix pomatia snails received intraauricular injections of 50 or 100mcg methionine-enkephalin, 100mcg naloxone, 100mcg naloxone plus 100mcg methionine-enkephalin, or saline. The dopamine (DA) and homovanillic acid (HVA) contents of ganglia were analyzed 40 minutes later. Results showed that methionine-enkephalin produced a dose dependent increase in DA and HVA contents and that this effect was antagonized by naloxone. Naloxone alone

had no significant effect. These findings suggest that opiate receptors are present in invertebrates. 6 references.

**002919** Otten, U.; Baumann, J. B.; Girard, J. Dept. of Endocrinology, University Children's Hospital, CH-4058 Basel, Switzerland **Stimulation of the pituitary-adrenocortical axis by nerve growth factor.** Nature. 282(5737):413-414, 1979.

The effect of systemic administration of nerve growth factor (NGF) on the hypothalamo/pituitary/adrenal axis was investigated. NGF induced an enhanced secretion of adrenocorticotropin (ACTH) and a prolonged increase in plasma glucocorticoid concentration after intravenous injection. The implications for the biological activity of NGF of these effects are discussed. These results, together with the observation that intracerebral injection of NGF induces an increased drinking response, indicate that NGF can affect both central and peripheral nervous systems. 16 references. (Author abstract modified)

**002920** Overstreet, D. H.; Russell, R. W.; Helps, S. C.; Runge, P.; Prescott, A. M. Flinders University of South Australia, School of Biological Sciences, Bedford Park, South Australia, 5042, Australia **Sex differences following pharmacological manipulation of the cholinergic system by DFP and philocarpine.** Psychopharmacology. 61(1):49-58, 1979.

The mechanisms responsible for sex differences in the effects of DFP, an irreversible anticholinesterase, on behavioral and physiological variables were investigated. It was found that female rats were more resistant than males to the effects of DFP: decreases in body temperature and water intake were significantly less in the females. In contrast, female rats were more sensitive to the hypothermic effects of pilocarpine, a directly acting muscarinic agonist, indicating that the resistance of females to the hypothermic effects of DFP cannot be attributed to decreased sensitivity of muscarinic cholinergic receptors. The experiments suggest that female rats may be less sensitive to the effects of DFP because they have higher levels of serum cholinesterase, which can bind to DFP administered peripherally and reduce the amount available for penetration into the brain. The results also support the hypothesis that the behavioral and physiological effects of DFP are related to the anticholinesterase properties of the agent. 40 references. (Author abstract modified)

**002921** Palacios, Jose M.; Niehoff, Debra L.; Kuhar, Michael J. Kuhar: Dept. of Pharmacology, Johns Hopkins University School of Medicine, 725 North Wolfe St., Baltimore, MD 21205 **Ontogeny of GABA and benzodiazepine receptors: effects of Triton X-100, bromide and muscimol.** Brain Research. 179(2):390-395, 1979.

The ontogeny of benzodiazepine (BZ) and GABA receptors was examined in Sprague-Dalwley rat brain. The effects of bromide and muscimol on BZ binding sites and the effect of Triton X-100 on GABA binding sites were also studied throughout development. Results suggest that the BZ binding site, the anionic site, and the site through which muscimol exerts its effects on BZ binding comprise an interacting system that is separate from high affinity GABA receptor mechanisms. 25 references.

**002922** Pare, William P. Pavlovian Research Laboratory, Veterans Administration Medical Center, Perry Point, MD 21902 **Atropine sulfate and incidence of activity-stress ulcers in the rat.** Communications in Psychopharmacology. 3(4):253-259, 1979.

Rats housed in running wheel activity cages were injected twice daily with either 2, 4, or 8mg/kg of atropine sulfate to investigate the effects of atropine sulfate on incidence of activity stress ulcers in the rat. It was hypothesized that atropine injected rats would show a significant reduction in the incidence of activity stress ulcers as compared to placebo and nondrug control rats. Activity stress ulcers were observed in all atropine injected rats and these animals also died sooner than placebo and nondrug control rats. It is suggested that stress ulcers resulted, not from an increase in gastric acid secretion, but from other factors such as a change in gastric microcirculation or an increase in gastric motility. 37 references. (Author abstract modified)

**002923** Patel, P. D.; Shah, D. S.; Patel, S. R.; Gulati, O. D. Dept. of Biochemistry and Biophysics, McGaw Medical Center, 2160 S. First Avenue, Maywood, IL 60153 **Investigation of the mechanism of decreased sensitivity of the rat seminal vesicle to norepinephrine by lithium.** Pharmacology. 18(2):64-71, 1979.

The mechanism by which lithium (Li) reduces the sensitivity of alpha-adrenergic receptors to norepinephrine (NE) was examined in the rat isolated seminal vesicle. In innervated preparations, Li shifted the concentration/response curves of NE, methoxamine, acetylcholine (ACh), and barium chloride to the right and reduced their maximum responses; antagonized the leftward shift and enhancement of maximum responses to NE by cocaine; and reduced only the maximum responses to potassium chloride (KCl). In denervated preparations, Li shifted the concentration/response curve of NE to the left without altering maximum responses. The antagonistic effects of Li on maximal responses to NE, ACh, and KCl in innervated preparations were significantly increased in calcium free medium. Li significantly increased NE uptake by the seminal vesicle. It is concluded that the Li-induced decrease in sensitivity to NE may be due to an increase in the uptake of NE and to a nonspecific postsynaptic spasmolytic action. 25 references. (Author abstract modified)

**002924** Paul, Steven M.; Crews, Fulton T. Clinical Psychobiology Branch, NIMH, Bethesda, MD 20205 **Rapid desensitization of cerebral cortical beta-adrenergic receptors induced by desmethylimipramine and phenoxybenzamine.** European Journal of Pharmacology. 62(4):349-350, 1980.

Combined administration of the antidepressant desmethylimipramine (DMI) and the irreversible alpha-adrenergic blocker phenoxybanzamine (PBZ) produced a rapid desensitization of cerebral cortical beta-adrenergic receptors in male Sprague-Dawley rats. A significant decrease in receptor density was observed after 6 days of treatment with DMI alone or as early as 24 hours after DMI combined with PBZ. The decrease in receptor density after 2 to 3 days of DMI and PBS was as great as that seen after 12 days of DMI alone. The combination of DMI and PBZ also caused a significantly greater decrease in beta-adrenergic receptors on day 12 than did DMI alone. 4 references.

**002925** Paul, Steven M.; Marangos, Paul J.; Goodwin, Frederick K.; Skolnick, Phil. Clinical Psychobiology Branch, NIMH, Bethesda, MD 20205 **Brain-specific benzodiazepine receptors and putative endogenous benzodiazepine-like compounds.** Biological Psychiatry. 15(3):407-428, 1980.

The pharmacological and physiological actions of benzodiazepine receptors and benzodiazepine-like compounds were investigated with rats. A highly significant correlation was found between the occupation of the binding sites by various benzodiazepines and their clinical effects. Results further support the physiolgical significance of the benzodiazepine receptor since brain specific receptors can be demonstrated in the intact animal under physiological conditions. The isolation of a number of substances from bovine brain that competitively inhibit 3H-diazepam binding to synaptosomal membranes suggest the presence of an endogenous ligand. It is concluded that results support the

existence in the brain of endogenous benzodiazepine-like compounds that could normally be involved in ameliorating anxiety and/or seizure activity. 25 references. (Author abstract modified)

**002926** Pavlik, Alfred; Teisinger, Jan. Institute of Physiology, Czechoslovak Academy of Sciences, Prague, Czechoslovakia **Effect of cycloheximide administered to rats in early postnatal life: prolonged inhibition of DNA synthesis in the developing brain.** Brain Research. 192(2):531-541, 1980.

Short-term inhibition of protein synthesis produced a prolonged inhibition of DNA synthesis and altered cell proliferation in the developing male hooded Druckray rat brain. Brain protein synthesis was inhibited by 75% after a single 0.6mg/kg dose of cycloheximide in 7-day-old rats, but the rate of protein synthesis returned to normal within 48 hours. The inhibition of DNA synthesis was greater and longer lasting in the forebrain and olfactory bulbs than in the cerebellum. DNA accumulation was retarded in the forebrain and cerebellum 72 hours after cycloheximide. 31 references. (Author abstract modified)

**002927** Pazo, Jorge H. 2da Catedra de Fisiologia Humana, Facultad de Medicina, Universidad de Buenos Aires, Paraguay 2155, 1121-Buenos Aires, Argentina **Effects of melatonin on spontaneous and evoked neuronal activity in the mesencephalic reticular formation.** Brain Research Bulletin. 4(6):725-730, 1979.

The acute effects of melatonin on the spontaneous activity of single cells in the mesencephalic reticular formation were studied in 40 male rats unanesthetized and immobilized with Flaxedil. One hundred and ten neurons were explored. Only 64 modified their spontaneous activity after the intravenous administration of melatonin. This response consisted of an increase in neural firing (six neurons), decrease (55 neurons) and biphasic response of decrease and increase (three neurons). When the effect of melatonin on the evoked activity in the mesencephalic neurons by peripheral stimulation (sciatic and photic) was checked, and increase of the number of neurons that showed inhibitory responses to photic stimulation was found. No changes in blood pressure and EEG were observed at the doses of melatonin used (200 to 600mcg/100g body weight). However, with doses of 60mcg, a tendency toward synchronization was observed in EEGs. The present observations indicate an inhibitory effect of melatonin on the spontaneous neuronal activity of the mesencephalic reticular formation. This effect may contribute to the changes in the sleep/wakefulness cycle and anticonvulsant action attributed to this hormone. 18 references. (Author abstract)

**002928** Perlow, Mark J.; Chiueh, C. C.; Lake, C. Raymond; Wyatt, Richard Jed. Division of Special Mental Health Research, Intramural Research Program, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Increased dopamine and norepinephrine concentrations in primate CSF following amphetamine and phenylethylamine administration.** Brain Research. 186(2):469-473, 1980.

Intramuscular administration of amphetamine or phenylethylamine (PEA) significantly increased the concentration of dopamine and norepinephrine in the CSF of adult male rhesus monkeys. The time course of the change in the CSF concentrations of the catchoalmines corresponded to the relative duration of action of amphetamine and PEA. Differences in the metabolism of PEA and amphetamine are discussed. 21 references.

**002929** Petersen, Erling N. A/S Ferrosan, Research Division, Sydmarken 5 DK 2860 Soborg, Denmark **The interaction of desipramine and the 5-HT uptake inhibitors femoxetine and paroxetine with the acute hypotensive effect of guanethidine in conscious spontaneously hypertensive rats.** Journal of Pharmacy and Pharmacology. 31(9):638-640, 1979.

The influence of desipramine, femoxetine, and paroxetine on the acute hypotensive effect of guanethidine were examined in spontaneously hypertensive male rats. Pretreatment with desipramine (1mg/kg i.v.) totally blocked the response to guanethidine, and pretreatment with 5mg/kg femoxetine or paroxetine partially antagonized the antihypertensive effect. None of the three test drugs reversed the guanethidine effect when given 15 and 30 minutes after guanethidine. Results suggest that serotonin uptake inhibitors such as femoxetine and paroxetine may be preferrable to noradrenaline uptake inhibiting drugs in depressed patients with hypertension controlled by guanethidine. 10 references.

**002930** Pettibone, Douglas J.; Wurtman, Richard J. Wurtman: 56-245, Massachusetts Institute of Technology, Cambridge, MA 02139 **D-amphetamine reduces striatal substance P concentrations by presynaptic release of dopamine.** Brain Research. 186(2):409-419, 1980.

Single doses of d-amphetamine sulfate caused dose dependent reductions in substance-P (SP) immunoreactive material in the striatum of male Sprague-Dawley rats, but repeated administration had no significant effect on striatal SP. SP levels were reduced from 1.37 to 0.97pmol/10mg tissue 2 hours after i.p. injection of 10mg/kg d-amphetamine. Similar reductions in striatal SP levels were observed after administration of 50 to 100mg/kg methylphenidate. No changes in SP concentrations were seen in the substantia nigra or hypothalamus after d-amphetamine treatment. The amphetamine-induced decline in striatal SP was blocked by pretreatment with alpha-methyltyrosine methyl ester (225mg/kg i.p.) or haloperidol (1, 3, or 10mg/kg i.p.) and by 6-hydroxydopamine lesions of the dopaminergic nigrostriatal tract. Results indicate that d-amphetamine lowers striatal SP levels through a mechanism involving presynaptic release of dopamine from the terminals of nigrostriatal neurons. 31 references. (Author abstract modified)

**002931** Phillis, J. W.; Edstrom, J. P.; Kostopoulos, G. K.; Kirkpatrick, J. R. Dept. of Physiology, College of Medicine, University of Saskatchewan, Saskatoon, Saskatchewan, Canada **Effects of adenosine and adenine nucleotides on synaptic transmission in the cerebral cortex.** Canadian Journal of Physiology and Pharmacology. 57(11):1289-1312, 1979.

The effects of adenosine and adenine nucleotides on synaptic transmission in the cerebral cortex were examined in the rat. Adenosine and adenine nucleotides had a potent depressive action on cerebral cortical neurons, including identified corticospinal cells. Other purine and pyrimidine nucleotides were either weakly depressant (inosine and guanosine derivatives) or largely inactive (xanthine, cytidine, thymidine, uridine derivatives). The 5′-triphosphates and to a lesser extent the 5′-diphosphates of all the purine and pyrimidines tested had excitant actions on cortical neurons. Adenosine transport blockers and deaminase inhibitors depressed firing of cortical neurons and potentiated the depressant actions of adenosine and adenine nucleotides. Methylxanthines (theophylline, caffeine, isobutylmethylxanthine) antagonized adenosine and adenine nucleotides and enhanced spontaneous firing rates. Adenosine 5′-monophosphate was found to hyperpolarize cerebral cortical neurons and suppress spontaneous and evoked excitatory postsynaptic potentials in the absence of any pronounced alterations in membrane resistance of the threshold for action potential generation. 78 references. (Author abstract modified)

**002932** Piercey, M. F.; Einspahr, F. J. Upjohn Company, Kalamazoo, MI 49001 **Use of substance P partial fragments to charac-**

**terize substance P receptors of cat dorsal horn neurons.** Brain Research. 187(2):481-486, 1980.

A study of the effects of substance-P (SP) and SP analogs on single neurons in the cat dorsal horn showed that SP and its analogs excite specific dorsal horn neurons through a common receptor. The slow time course of SP's excitatory effects was not due to its degradation to a smaller, more rapidly acting fragment; the smallest active fragments elicited the same slow excitatory effect as SP. It is concluded that the dorsal horn SP receptor is similar to those in motoneurons, gastrointestinal tract, and blood vessels, but may have some unique properties. 19 references.

**002933** Piercey, Montford F.; Einspahr, Fred J.; Dobry, Peggy J. K.; Schroeder, Lawrence A.; Hollister, Rusel P. Upjohn Company, Kalamazoo, MI 49001 **Morphine does not antagonize the substance P mediated excitation of dorsal horn neurons.** Brain Research. 186(2):421-434, 1980.

Multibarrelled microelectrodes were used to test the effects of iontophoretically released substance-P (SP), morphine, glutamate, and naloxone on cat spinal cord dorsal horn neurons. Cells excited by SP were also excited by noxious stimuli, suggesting SP is released by primary nociceptor afferents to excite dorsal horn neurons. Iontophoretic morphine did not antagonize the SP-induced discharges and frequently potentiated the SP response. Iontophoretic morphine also frequently increased the spontaneous activity of dorsal horn neurons, as well as the activity evoked in these cells by noxious cutaneous heat and by glutamate. Naloxone did not antagonize these effects. Intravenous morphine depressed spontaneous discharges, but iontophoretic morphine produced excitatory effects even in spinal animals pretreated with analgesic doses of intravenous morphine. Intravenous morphine did not depress the response to SP in dorsal horn neurons and failed to antagonize the effects of SP in peripheral systems. Results indicate that morphine is not an SP receptor antagonist. 54 references. (Author abstract modified)

**002934** Placheta, Peter; Karobath, Manfred. Institute of Pharmacology, University of Vienna, Wahringerstrasse 13a, A-1090 Vienna, Austria **In vitro modulation by SQ 20009 and SQ 65396 of GABA receptor binding in rat CNS membranes.** European Journal of Pharmacology. 62(2/3):225-228, 1980.

Two new pyrazolopyridines with anxiolytic properties in animals, SQ-20009 and SQ-65396, reversibly increased sodium independent 3H-GABA binding to Sprague-Dawley rat cerebral cortex membranes. This modulation was sensitive to Triton-X 100 and partially dependent on chloride. Kinetic analysis of 3H-muscimol binding revealed an increase in the apparent number of binding sites. Results suggest a functional association between sodium independent GABA binding sites and the GABA/benzodiazepine receptor complex. 10 references. (Author abstract modified)

**002935** Poddar, M. K.; Urquhart, D; Sinha, A. K. Dept. of Physiology and Biophysics, College of Medicine and Dentistry of New Jersey, Rutgers Medical School, Piscataway, NJ 08854 **Diazepam binding in brain after sleep and wakefulness.** Brain Research. 193(2):519-528, 1980.

Membranes prepared from various regions of male golden hamster brain following 50 minutes of nonREM sleep or a comparable period of wakefulness showed no significant differences in (3H)diazepam binding. However, (3H)diazepam binding in all brain areas, particular the cerebral cortex, was reduced by the 30,000xg supernatant from awake brain, but not by supernatant from sleeping brain. Scatchard analysis indicated that in the presence of supernatant from awake brain, the affinity of the receptor for (3H) diazepam decreased significantly, with no change in the maximum number of binding sites. Results suggest the presence of a benzodiazepine binding inhibitor, possibly an endogenous benzodiazepine-like substance, in the supernatant from awake animals. 22 references. (Author abstract modified)

**002936** Polc, P. Pharma Research Dept., Area I, F. Hoffmann-La Roche & Co. Ltd.,@ Grenzacherstrasse 124, CH-4002 Basel, Switzerland **Effects of GABA-mimetic agents on the cat spinal cord.** Progress in Neuro-Psychopharmacology. 3(4):345-352, 1979.

The effects of muscimol, ibotenic acid, isoguvacine, 4,5,6,7-tetrahydroisoxazolo(5,4-c)pyridin-3-ol (THIP), and GABA on the lumbosacral spinal cord of spinal cats were examined. Following i.v. administration, these GABA mimetic agents enhanced the excitability of primary afferents and the amplitude of dorsal root reflexes. Segmental monosynaptic ventral root reflexes and dorsal root potentials were depressed, as were the spontaneous gamma fiber activities and the excitability of motoneurons and polysynaptic reflexes. Muscimol was the most potent compound, followed by ibotenic acid, isoguvacine and THIP, and GABA. Most effects were reversibly antagonized by bicuculline, but not by strychnine. Results suggest that GABA mimetic agents alter spinal cord activity by actions related to GABA receptors located on primary afferent endings, intrinsic spinal neurons, and motoneurons. 26 references. (Author abstract modified)

**002937** Prange, A. J., Jr.; Nemeroff, C. B.; Bissette, G.; Manberg, P. J.; Osbahr, A. J., III; Burnett, G. B.; Loosen, P. T.; Kraemer, G. W. Biological Sciences Research Ctr., Dept. of Psychiatry, University of North Carolina School of Medicine, Chapel Hill, NC 27514 **Neurotensin: distribution of hypothermic response in mallian and submammalian vertebrates.** Pharmacology Biochemistry and Behavior. 11(5):473-477, 1979.

The effect of neurotensin (NT), an endogenous tridecapeptide, on thermoregulatory processes was investigated in a variety of mammalian and nonmammalian vertebrates. These were the bluegill, frog, lizard, pigeon, ground squirrel, woodchuck, golden hamster, rabbit, guinea-pig, gerbil, mouse, rat, and rhesus monkey. All species except monkey were tested in two ambient temperatures, 23 degrees C and 4 degrees C, except poikilotherms, over a 2 hour period following injection with NT. No significant alteration was induced in any of the poikilotherms studied. At 23 degrees C, NT produced a significant hypothermic response in the mouse, rat, gerbil, and monkey, with no effect observed in the pigeon, rabbit, guinea-pig, golden hamster, ground squirrel, or wood chuck. At 4 degrees C, NT produced a significant decrease in body temperature in the mouse, rat, gerbil, guinea pig, and golden hamster, with no effect evident in the pigeon, rabbit, ground squirrel, or woodchuck. Species known to respond to cold by increasing metabolic rate appear to be most responsive to NT. The hypothermic activity of NT in a variety of mammals suggests that the peptide may play a role in thermoregulation and its disorders. 22 references. (Author abstract modified)

**002938** Pugsley, T. A.; Lippmann, W. Biochemical Pharmacology Dept., Ayerst Research Laboratories, Box 6115, Montreal, Quebec H3C 3JI, Canada **Effect of acute and chronic treatment of tandamine, a new heterocyclic antidepressant, on biogenic amine metabolism and related activities.** Naunyn-Schmiedeberg's Archives of Pharmacology. 308(3):239-247, 1979.

The effects of acute (10mg/kg i.p.) and chronic (10mg/kg/day i.p. for 21 days) treatment with tandamine, a clinically effective heterocyclic antidepressant, on biogenic amine uptake and metabolism were examined in male Sprague-Dawley rats. Like desipramine, tandamine blocked norepinephrine (NE)

uptake in brain and heart after acute or chronic treatment, but did not alter dopamine (DA) or serotonin (5-HT) uptake. Both drugs lowered endogenous brain NE when given chronically but not acutely, and neither drug altered brain DA and 5-HT or heart NE levels. Chronic treatment with tandamine also appeared to increase NE turnover. Tandamine and desipramine both increased the behavioral effects of L-dopa in male Swiss mice, but tandamine was more effective than desipramine at the lowest dose examined (10mg/kg). Tandamine was 57 to 833 times less effective in binding to rat brain muscarinic receptors than desipramine, imipramine, butriptyline, and amitriptyline. Results indicate that tandamine resembles desipramine in its action on biogenic amines, but differs in having only slight anticholinergic properties. 42 references. (Author abstract modified)

**002939** Pyornila, A.; Lahti, H.; Hissa, R. Dept. of Zoology, Zoophysiological Laboratory, University of Oulu, Oulu, Finland **The influence of intrahypothalamically injected cholinergic agents on temperature regulation in the pigeon at ambient temperatures of 20 degrees, 32 degrees, and 38 degrees C.** Neuropharmacology. 18(5):503-510, 1979.

The effects of intrahypothalamic injections of cholinergic agents on temperature regulation in unanesthetized pigeons were studied at ambient temperatures of 20, 32, and 38 degrees C. Studies with acetylcholine, physostigmine, oxotremorine, and carbamylcholine suggest that cholinergic stimulation of the hypothalamus inhibits thermoregulatory responses (both shivering and panting) elicited by external changes in temperature. In a thermoneutral environment, the cholinergic agents evoked a slight hyperthermia. The neuronal pathways involved in these responses appeared to be muscarinic. 23 references. (Author abstract modified)

**002940** Quattrone, A.; Schettini, G; Di Renzo, G. F.; Preziosi, P. Dept. of Neurology, 11th Faculty of Medicine, Piazza Miraglia 2, University of Naples, Naples, Italy **Pharmacological evidence of an interaction between serotonergic and dopaminergic neurons in the control of prolactin secretion in male rats.** Archives Internationales de Pharmacodynamie et de Therapie. 238(1):42-49, 1979.

Penfluridol and alpha-methyl-p-tyrosine (a-MPT) significantly stimulated secretion of prolactin (PRL) in male Wistar rats. Quipazine also increased plasma PRL levels, but was not able to further stimulate PRL release in animals pretreated with penfluridol or a-MPT. D-fenfluramine increased plasma PRL levels, but did not further stimulate PRL secretion in rats pretreated with penfluridol. Results indicate that serotonin may stimulate PRL release through an inhibition of dopaminergic neurons. 30 references. (Author abstract modified)

**002941** Raisman, Rita; Briley, Michael S.; Langer, Salomon Z. Dept. of Biology, Synthelabo, LERS, 58, rue de la Glaciere, F-75013 Paris, France **Specific tricyclic antidepressant binding sites in rat brain characterized by high-affinity 3H-imipramine binding.** European Journal of Pharmacology. 61(4):373-380, 1980.

The specific binding of 3H-imipramine to homogenates of various regions of male Sprague-Dawley rat brain was rapid, reversible, and of high affinity. It was inhibited by tricyclic antidepressants at nanomolar concentrations and by atypical antidepressants at micromolar concentrations. The number of specific 3H-imipramine binding sites in the cortex was significantly reduced by treatment with desipramine for 3 weeks. These 3H-imipramine binding sites may be important in the study of depression and antidepressant drugs. 26 references. (Author abstract modified)

**002942** Ramm, Peter; Taub, Hillel. Dept. of Psychology, Queen's University, Kingston, Ontario K7L 3N6 Canada **Enhancement of tyrosine hydroxylase activity by oxotremorine does not affect sleep in the rat.** Pharmacology Biochemistry and Behavior. 12(3):353-357, 1980.

The influence of the enhancement of tyrosine hydroxylase (TH) activity by oxotremorine in the rostral pons of rats on sleep behavior was investigated. Marked enhancement of TH activity was observed in the rostral pons of Wistar albino rats, 3 days after a single injection of oxotremorine. TH activity in other brain areas, and regional levels of norepinephrine, dopamine, serotonin, and 5-hydroxyindoleacetic acid were unaffected. Enhancement of TH activity did not affect length or number of REM episodes, or the amount of REM occurring in 24hr. REM occurrence did not, thus, vary in accordance with activity of the rate limiting enzyme catecholamine synthesis. These data suggest that, although REM may reflect neuronal protein synthesis, REM is not part of a mechanism regulating the activity of enzymes in the pontine catecholamine synthesis pathway. 50 references. (Author abstract modified)

**002943** Ramsay, R. Eugene; Hammond, Edward J.; Perchalski, Robert J.; Wilder, B. Joe. Neurology Service (127), Veterans Administration Hospital, 1201 NW 16th Street, Miami, FL 33125 **Brain uptake of phenytoin, phenobarbital, and diazepam.** Archives of Neurology. 36(9):535-539, 1979.

Penetration of phenytoin, phenobarbital, and diazepam into the parenchyma of the cat brain was assessed after intravenous infusion. Maximum brain concentrations were reached at 1 minute (diazepam), 3 minutes (phenobarbital), and 6 minutes (phenytoin). Phenobarbital and phenytoin entered more slowly, but remained bound with similar brain concentrations at 1 minute and 60 minutes. Relatively free movement of diazepam in and out of the brain was found, with lower brain concentrations occuring 45 to 60 minutes after infusion. Peak phenytoin concentration occurred in the brain and CSF at the same time (6 minutes), and constant plasma/CSF ratios were found after 6 minutes. The treatment of status epilepticus as indicated by the drug kinetics would be: 1) initial use of i.v. diazepam to effect immediate seizure control due to more rapid penetration into the brain; and 2) subsequent rapid use of i.v. phenytoin or phenobarbital to maintain seizure control due to relative slow clearance of these drugs out of the brain, while diazepam has a quite rapid clearance. 19 references. (Author abstract modified)

**002944** Rea, M. A.; McBride, W. J.; Rohde, B. H. Dept. of Psychiatry, Institute of Psychiatric Research, Indiana University School of Medicine, Indianapolis, IN 46223 **Regional and synaptosomal levels of amino acid neurotransmitters in the 3-acetylpyridine deafferentated rat cerebellum.** Journal of Neurochemistry. 34(5):1106-1108, 1980.

Regional and synaptosomal levels of amino acid neurotransmitters (aspartate, glutamate, taurine, GABA, and alanine) were measured in the 3-acetylpyridine (3-AP) deafferentated rat cerebellum. Control rats and rats administered a single i.p. injection of 3-AP (65mg/kg) were killed by decapitation 14 days and 21 days postinjection. The levels of aspartate and taurine were significantly lower in all three regions of the cerebellum (cortex, white matter, nuclei) of 3-AP injected rats. Furthermore, a reduction in the level of aspartate and taurine by 3-AP was also found in the crude synaptosomal fraction. The levels of glutamate, GABA, and alanine in the three regions were, in general, not altered by treatment with 3-AP, but the level of glutamate in the P2 fraction was reduced after drug treatment. Implications of the results for identification of the neurotransmitter released from the olivocerebellar projection are discussed. 23 references.

**002945** Reading, Harold W.; Isbir, Turgay. MRC Brain Metabolism Unit, Thomas Clouston Clinic, 153 Morningside Drive, Edinburgh EH10 5LG, Scotland **Action of lithium on ATPases in the rat iris and visual cortex.** Biochemical Pharmacology. 28(23):3471-3474, 1979.

The effects of lithium on adenosine triphosphatase (ATPase) in the rat iris and visual cortex were examined with male Wistar rats. The experimental rats were given a diet with lithium chloride for periods up to 4 weeks. Control animals received the diet without lithium salt, and all animals were given a choice of 0.9% sodium chloride solution or water to drink. The use of 60mM LiCl/kg in the food produced plasma lithium concentrations comparable to therapeutic levels in humans. In both iris and visual cortex, lithium treatment produced an increase in Mg2 activated and Ca2/Mg2 activated ATPase activities. It is concluded that the major effects of lithium administration in a variety of tissues appear to be confined to calcium and magnesium activated ATPase with very little action on sodium pump ATPase. 15 references.

**002946** Rebec, George V.; Bashore, Theodore R.; Zimmerman, Kenneth S.; Alloway, Kevin D. Dept. of Psychology, Indiana University, Bloomington, IN 47405 **differential antagonism of amphetamine- and apomorphine-induced alterations of spontaneous neuronal activity in the neostriatum and nucleus accumbens.** Pharmacology Biochemistry and Behavior. 11(5):529-538, 1979.

The ability of clozapine and haloperidol to antagonize the depression of firing rate produced by d-amphetamine and apomorphine in the neostriatum and nucleus accumbens was tested in immobilized, locally anesthetized rats. In the neostriatum, an intraperitoneal injection of 2.5mg/kg d-amphetamine or 1.0mg/kg apomorphine produced a prolonged inhibition of neuronal activity that was reversed by a subsequent injection of either 20mg/kg clozapine or 2.0mg/kg haloperidol. An analysis of the onset and magnitude of the blockade revealed the clozapine was more effective than haloperidol in reversing the amphetamine response but that both antipsychotic drugs produced a comparable blockade of the apomorphine-induced depression. Similar results were obtained in the nucleus accumbens. The data indicate that although clozapine acts equieffectively in the neostriatum and nucleus accumbens, this atypical antipsychotic drug, aside from blocking postsynaptic dopamine receptors, may exert at least some of its effects by preventing dopamine release. 55 references. (Author abstract modified)

**002947** Reggiani, Angelo; Battaini, Fiorenzo; Kobayashi, Hideyuki; Spano, Pierfranco; Trabucchi, Marco. Dept. of Pharmacology and Pharmacognosy, University of Milan, Via Vanvitelli, 32, I-20129 Milan, Italy **Genotype-dependent sensitivity to morphine: role of different opiate receptor populations.** Brain Research. 189(1):289-294, 1980.

Morphine (5 or 10mg/kg i.p. ) increased striatal and limbic levels of dihydroxyphenylacetic acid in C57/6j mice, but did not alter levels of the dopamine (DA) metabolite in DBA/2j mice. When tritiated D-Ala2-Met-enkephalin or leu-enkephalin were used as ligands, striatal opiate receptor binding was lower in DBA mice than in C57 mice, due to a smaller number of receptor sites in the DBA mice. No strain differences in opiate receptor binding were found in other brain regions. Results suggest that the effects of morphine on DA metabolism are mediated by opiate receptors located on dopaminergic terminals. 27 references.

**002948** Reisine, T. D.; U'Prichard, D. C.; Wiech, N. L.; Ursillo, R. C.; Yamamura, H. I. Yamamura: College of Medicine, University of Arizona Health Sciences Center, Tucson, AZ 85724 **Effects of combined administration of amphetamine and iprindole on brain adrenergic receptors.** Brain Research. 188(2):587-592, 1980.

Combined treatment with 20mg/kg/day amphetamine and 25mg/kg/day iprindole for 3 days significantly reduced the density of cortical beta-adrenergic receptors in male CD rats. The density of these receptors was not significantly altered by treatment with either drug alone. All three drug treatments significantly elevated alpha2-adrenergic receptor densities, without affecting the properties of alphal-adrenergic receptors. 19 references.

**002949** Ribeiro-da-Silva, A.; Coimbra, Antonio. Institute of Histology and Embryology, Faculty of Medicine of Oporto, Oporto, Portugal **Neuronal uptake of (3H)GABA and (3H)glycine in laminae I-III (substantia gelatinosa rolandi) of the rat spinal cord. An autoradiographic study.** Brain Research. 188(2):449-464, 1980.

The neuronal uptake of (3H)GABA and (3H)glycine in laminae I-III of the rat spinal cord was examined after injection of the isotopes into the subarachnoid space. Light microscope autoradiographs of transverse cord sections showed dense labeling over lamina-I for GABA and over lamina-II for glycine. Nerve cell bodies were labeled in lamina-I of the (3H)GABA treated animals and in lamina-III of (3H)glycine treated rats. Results indicate there are two types of inhibitory interneurons in the rat substantia gelatinosa, a GABAergic interneuron with cell body in lamina-I and a glycinergic interneuron in lamina-III. 36 references. (Author abstract modified)

**002950** Riblet, L. A.; Gatewood, C. F.; Mayol, R. F. Department of Biologic Research, Mead Johnson Pharmaceutical Division, Evansville, IN 47721 **Comparative effects of trazodone and tricyclic antidepressants on uptake of selected neurotransmitters by isolated rat brain synaptosomes.** Psychopharmacology. 63(2):99-101, 1979.

The effect of trazodone, a new antidepressant agent, on uptake of serotonin (5-HT), norepinephrine (NE), and dopamine (DA) by crude synaptosome preparations from rat hypothalamus was compared with those of imipramine, desipramine, and clomipramine. Trazodone was determined to be a very selective inhibitor of the 5-HT uptake mechanism. Clomipramine was the only other selective inhibitor of 5-HT uptake. Although less potent, trazodone was 4 times more selective than clomipramine in its ability to inhibit synaptosomal uptake of 5-HT with respect to NE. This selectivity for the 5-HT uptake mechanism is consistent with the clinical antidepressant efficacy of trazodone. 18 references. (Author abstract modified)

**002951** Rips, Richard; Desiles, Marguerite; Puech, Alain J. INSERM, Unite de Pharmacologie Chimique, 17, rue du Fer a Moulin, F-75005 Paris, France **Is a dopaminergic system involved in thyrotropin releasing hormone induced hyperthermia and in its potentiation by amphetamine?** Progress in Neuro-Psychopharmacology. 3(4):337-344, 1979.

Intraperitoneally administered thyrotropin releasing hormone (TRH) produced a dose related hyperthermia in female Swiss mice. This effect was potentiated by amphetamine at doses that usually cause hypothermia. The hyperthermia induced by TRH was also potentiated by p-chloroamphetamine and L-dopa, but not by apomorphine. The TRH hyperthermia was significantly reduced by alpha-methyl-tyrosine and haloperidol, but not by pimozide or chlorpromazine. The hyperthermia induced by TRH in combination with amphetamine was not reduced by any of the dopamine antagonists tested, even at doses that reverse amphetamine hyperthermia. Results suggest that dopamine receptors do not participate directly in the hyperthermia caused

by TRH or in its potentiation by amphetamine. 27 references. (Author abstract modified)

**002952** Robert, Timothy Albert. East Tennessee State University **Enantiomeric influences in neuroleptic binding to models of the dopamine receptor. (Ph.D. dissertation).** Dissertation Abstracts International. 40(7):3116-B, 1980. Ann Arbor, Univ. Microfilms No. 8001356, 94p., 1979.

The in vitro dopaminergic effects of optically active phenotiazine derivatives were examined. Binding studies were performed in calf caudate nucleus homogenates with () and (-) methotrimeprazine, () and (-) thioridazine, () and (plus or minus) promethazine, () and (-) dioxopromethazine, and () and (-) P-892. A significant isomeric effect was observed only for the neuroleptics, thioridazine and methotrimeprazine, in displacing 3H-DA whereas 3H-SP competition exhibited stereospecificity with promethazine and dioxopromethazine as well. Isomer pairs differed in their magnitudes of stereospecificity between 3H-DA and 3H-SP displacement. In marked contrast to the radioligand binding results, DA/AC failed to exhibit an isomeric effect upon inhibition with methotrimeprazine. These observations suggest that the binding sites for dopamine agonists and antagonists associated with these in vitro models are all different molecular species. (Journal abstract modified)

**002953** Robertson, H. A. Dept. of Pharmacology, Sir Charles Tupper Medical Building, Dalhousie University, Halifax, Nova Scotia, Canada B3H 4H7 **Stimulation of 3H-apomorphine binding by dopamine and bromocriptine.** European Journal of Pharmacology. 61(2):209-211, 1980.

The effects of dopamine and bromocriptine on 3H-apomorphine binding by rat striatum/nucleus accumbens membranes were examined. Both drugs displaced 3h-apomorphine binding at low concentrations, but stimulated binding at high concentrations. The dopamine agonists lergotrile and dihydroxyergotamine also stimulated 3h-apomorphine binding. Ascorbate completely abolished the dopamine stimulated 3H-apomorphine binding. Results suggest that apomorphine may bind to two distinct sites on neuronal membranes. 4 references.

**002954** Robinson, Susan E.; Berney, Stuart; Mishra, Radhakanta; Sulser, Fridolin. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeth's Hospital, Washington, DC 20032 **The relative role of dopamine and norepinephrine receptor blockade in the action of antipsychotic drugs: metoclopramide, thiethylperazine, and molindone as pharmacological tools.** Psychopharmacology. 64(2):141-147, 1979.

A series of studies was conducted in the rat to futher delineate the role of striatal and limbic dopaminergic versus limbic noradrenergic blockade in the pharmacologic and therapeutic action of the antispsychotic drugs metoclopramide, thiethylperazine, and molindone. Metoclopramide, which shares many properties with the neuroleptics but is not an efficacious antipsychotic agent, was a potent blocker of dopamine (DA) receptors in both striatum and limbic forebrain (comparable in potency to that of chlorpromazine), as evidenced by the increase in homovanillic acid in both brain structures. In contrast, metoclopramide was a weak inhibitor of the norepinephrine (NE) receptor coupled adenylate cylcase system in the limbic forbrain. Molindone, which is reported not to block DA sensitive adenylate cyclase, was a potent in vivo blocker of DA receptors in both striatum and limbic forebrain, and also inhibited markedly the cyclic AMP response to NE in the limbic forebrain. The phenothiazine derivative, thiethylperazine, was also a potent blocker of DA receptors in both brain areas and displayed an IC50 for NE blockade in the limbic forebrain comparable to that of chlorpromazine. Results support the view that the ability and potency of drugs to block DA receptors parallels their ability and potency to cause extrapyramidal symptoms in man, and suggest that the blockade of NE receptors coupled adenylate cyclase systems in brain may be relevant to both pharmacological and therepeutic activity of antipsychotic drugs. 52 references. (Author abstract modified)

**002955** Rodrigues, P. S.; Martins-Ferreira, H. Martins-Ferreira: Instituto de Biofisica, Universidade Federal do Rio de Janeiro, Ilha do Fundao, 21910 Rio de Janeiro, Brazil **Cholinergic neurotransmission in retinal spreading depression.** Experimental Brain Research. 38(2):229-236, 1980.

The participation of cholinergic synapses in retinal spreading depression (SD) was demonstrated in white leghorn chicks. Acetylcholine (ACh) was liberated during SD. ACh elicited SD, and d-tubocurarine and atropine blocked this effect. Prostigmine triggered the reaction and potentiated the effect of ACh. The velocity of propagation was decreased by ACh and prostigmine. (Author abstract modified)

**002956** Roffman, M.; Reigle, T.; Orsulak, P.; Cassens, G.; Schildkraut, J. J. Dept. of Pharmacology, Ciba-Geigy Corporation, Summit, NJ 07901 **Further studies of the effects of morphine on the levels of MHPG-S04 in rat brain.** Neuropharmacology. 18(5):483-487, 1979.

Acute administration of morphine resulted in an increase in the levels of the norepinephrine metabolite 3-methoxy-4-hydroxyphenylglycol sulfate (MHPG-S04) in male Sprague-Dawley rat brain. Pretreatment with naloxone at doses that did not significantly alter MHPG-S04 attenuated the morphine-induced increase in MHPG-S04. The morphine-induced increase in MHPG-S04 was not due to drug induced blockade of the egress of the metabolite from the brain, since the rate of disappearance of MHPG-S04 after pargyline treatment was similar in morphine treated and control rats. Morphine did not inhibit the uptake of intracisternally administered 3H-norepinephrine and did not alter 3H-norepinephrine metabolism. Tolerance developed to the morphine-induced increase in MHPG-S04 levels with chronic administration, and MHPG-S04 levels were significantly decreased when chronic morphine treatment was terminated. 24 references. (Author abstract modified)

**002957** Rossowska, Magdalena. Polish Academy of Sciences Medical Research Centre, Dept. of Neurochemistry 3, Dworkowa str., 00-784 Warsaw, Poland **Studies on the glycoprotein component of (Na-K)ATPase from guinea pig brain.** Neurochemical Research. 4(6):723-729, 1979.

The mechanism of the brain microsomal (Na-K)ATPase inhibition was investigated, based on the assumption that the glycoprotein part of the enzyme is exposed on the outer membrane surface. The modification with concanavalin A of sugar end groups exposed by neuraminidase treatment resulted in a significant decrease of the brain (Na-K)ATPase activity. The percentage of the enzyme inhibition by concanavalin A binding to the neuraminidase treated prepartion corresponds to the amount of liberated sialic acids. The modification of the glycoprotein part of the brain (Na-K)ATPase complex by neuraminidase and concanavalin A treatments did not affect K-nitrophenylphosphatase activity. 13 references. (Author abstract)

**002958** Roth-Schechter, B. F.; Tholey, G.; Mandel, P. Institute de Chimie Biologique, Faculte de Medecine, 11 rue Humann, 67085 Strasbourg Cedex, France **Development and mechanism of barbiturate tolerance in glial cell cultures.** Neurochemical Research 4(1):83-97, 1979.

The effects of pentobarbital exposure on cellular respiration and on activities of enzymes involved in carbohydrate metabo-

lism were studied in glial cells in primary culture and in continuous clonal line. Biochemical tolerance to pentobarbital was demonstrated in both types of glial cells, response to the depressant effects of a challenge dose of pentobarbital on cellular repiration was attenuated in barbiturate cultivated cells compared to cells grown in drug free medium. Biochemical tolerance was evident in the presence of glucose and succinate, but not with malate as substrate. Tolerance to pentobarbital was accompanied by increased activities of hexokinase, glucose-6-phosphate dehydrogenase, succinate dehydrogenase, and glutamate dehydrogenase and by a marked increase in the number of glial cell mitochondria apparent in electron micrographs. Results suggest that glial cells compensate for the continuous presence of pentobarbital by accelerated glucose uptake and metabolism, accelerated succinate metabolism, and increased mitochondrial activity. 23 references. (Author abstract modified)

**002959** Roth, Jerome A.; Whittemore, Russell M.; Shakarjian, Michael P.; Eddy, Barbara J. Dept. of Pharmacology and Therapeutics, State University of New York, Buffalo, NY 14214 **Inhibition of human brain type A and B monoamine oxidase by chlorpromazine and metabolites.** Communications in Psychopharmacology. 3(4):235-243, 1979.

Clorpromazine and a variety of its hydroxylated and N-demethylated catabolites were found to inhibit both the A-forms and B-forms of brain monoamine oxidase (MAO). All the phenothiazine durgs tested, with the exception of chlorpromazine sulfoxide, which did not affect MAO activity, inhibited the A-form of MAO equal to or better than the type B-form of the oxidase. Compared to the tricyclic antidepressant drugs, chlorpromazine was the most effective inhibitor of the type-A species of MAO whereas the antidepressant drugs had higher affinities for the B-form of MAO. 20 references. (Author abtract)

**002960** Rowlands, Gethin J.; Roberts, Peter J. Roberts: School of Biochemical and Physiological Sciences, University of Southampton, Southampton, S09 3TU, England **Activation of dopamine receptors inhibits calcium-dependent glutamate release from cortico-striatal terminals in vitro.** European Journal of Pharmacology. 62(2/3):241-242, 1980.

Dopamine (DA) produced a marked, dose dependent inhibition of the release of glutamate from rat striatal slices in the presence of high potassium. The DA uptake inhibitor benztropine potentiated the inhibition by DA. Apomorphine and 3,4-dihydroxynomifensine also inhibited the evoked release of glutamate; noradrenaline, picrotoxin, and atropine had no effect on the response. Results suggest that a DA receptor located on glutamatergic presynaptic terminals in rat striatum modulates the release of transmitter from those terminals. 5 references.

**002961** Rubin, Jay J.; Willmore, L. James. College of Medicine, University of Florida, Gainesville, FL **Prevention of iron-induced epileptiform discharges in rats by treatment with antiperoxidants.** Experimental Neurology. 67(3):472-480, 1980.

Subpial injection of an aqueous solution of iron salts into CD rats isocortex resulted in epileptiform discharges in 94% of the animals. Pretreatment with the antioxidant alpha-tocopherol and with selenium prevented the development of iron-induced epileptiform activity in 72%. It is suggested that peroxidative injury may be an important mechanism in the development of posttraumatic epilepsy. 61 references. (Author abstract modified)

**002962** Rudeen, P. K.; Philo, R. C.; Symmes, S. K. Dept. of Anatomy, Bowman Gray School of Medicine, Winston-Salem, NC 27103 **Antiepileptic effects of melatonin in the pinealectomized Mongolian gerbil.** Epilepsia. 21(2):149-154, 1980.

The antiepileptic effects of melatonin in the pinealectomized Mongolian gerbil were investigated. Melatonin administered in the form of subcultaneous beeswax implants was given to gerbils 4 days prior to pinealectomy or sham pinealectomy. Beeswax pellets were implanted as the vehicle agent in respective groups. Melatonin treated pinealectomized animals exhibited fewer seizures than did pinealectomized animals that did not receive melatonin. The results indicate that melatonin has an ameliorative effect upon pinealectomy-induced seizures, but the mechanism by which pinealectomy induced the seizures, and the etiology in which melatonin reduces the seizure activity is unknown. 17 references. (Author abstract modified)

**002963** Russell, Roger W.; Carson, Virginia G.; Jope, Richard S.; Booth, Ruth A.; Macri, James. Flinders University of South Australia, Bedford Park, South Australia 5042 **Development of behavioral tolerance: a search for subcellular mechanisms.** Psychopharmacology. 66(2):155-158, 1979.

The possible involvement of certain subcellular events in the development of behavioral tolerance was examined in rats. The concentrations of acetylcholine (ACh) and choline (Ch), the high affinity transport of Ch, and the rate of synthesis of ACh were measured in synaptosomes prepared from the brains of rats. The assays were made at critical times during the acute changes in behavior induced by the administration of the anticholinesterase, di-isopropylfluorophosphate, and during the development of behavioral tolerance to this compound as chronicity of administration continued. No statistically significant differences were found among treatment groups in the total concentration of ACh or Ch, the synthesis of ACh, or the high affinity transport of Ch. These results, plus evidence from previous experiments, indicate that the development of behavioral tolerance does not relate to the factors studied. It is suggested that the possible involvement of mechanisms controlling the release of ACh, and changes in cholinergic (muscarinic) receptors, should be studied. 28 references. (Author abstract modified)

**002964** Sabato, Ulises C.; Fiszer-de-Plazas, Sara; De Robertis, Eduardo. Instituto de Biologia Celular, Facultad de Medicina, Universidad de Buenos Aires, (1121) Buenos Aires, Argentina **The convulsant drugs 3-mercaptopropionate and methionine sulfoximine inhibit L-glutamate and L-aspartate binding to a hydrophobic protein fraction from rat cerebral cortex.** Neurochemical Research. 4(6):713-722, 1979.

The action of the convulsant drugs, methionine sulfoximine (MSO), 3-mercaptopropionate (3-MP), megimide (MG), and allylglycine on the binding of L-(14C)aspartate, L-(14C)glutamate and (14C)GABA to a hydrophobic protein fraction isolated from rat cerebral cortex was investigated. Using the convulsant at .0001M concentration and the radioactive ligands at .000001M concentrations, the binding of L-(14C)glutamate was inhibited 60% by 3-MP and 40% by MSO, while MG and allylglycine had no effect. The binding of L-(14C)aspartate was inhibited 55%, and 10% to 20% by 3-MP and MSO, respectively, while MG and allylglycine had no effect. None of the drugs mentioned, except for a minimal inhibition by MG, altered the binding of (14C)GABA. Neither MSO nor 3-MP affected the high affinity sites for L-(14C)glutamate or L-(14C)aspartate, but they had a strong inhibitory action on the medium affinity site. These results are discussed in relation to the possible mechanism of action of these drugs on L-glutamate and L-aspartate receptors. 25 references. (Author abstract)

**002965** Sangdee, Chaichan; Franz, Donald N. Franz: Dept. of Pharmacology, College of Medicine, Chiang-Mai University, Chiang-Mai, Thailand **Enhancement of central norepinephrine and 5-hydroxytryptamine transmission by tricyclic antidepressants.** Psychopharmacology. 62(1):9-16, 1979.

The relative abilities of 1 to 3mg/kg of desipramine, imipramine, amitriptyline, and chlorimipramine to enhance synaptic transmission mediated by either norepinephrine (NE) or serotonin (5-HT) were determined by testing their effect directly on NE or 5-HT transmission to sympathetic preganglionic neurons in unanesthetized spinal rats. All four drugs enhanced transmission by both NE and 5-HT, but their relative selectivities for the two transmitters differed markedly and were complementary. The results support those of previous studies based on less direct methods for assessing inhibition of amine reuptake by tricyclic antidepressants. 36 references. (Author abstract modified)

**002966** Sarne, Yosef; Gothilf, Yehoshua; Weissman, Ben-Avi. Dept. of Physiology, Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel **Long-term interactions between endogenous and exogenous opiates.** European Journal of Pharmacology. 62(1):117-120, 1980.

The effects of morphine, humoral endorphin, and leucine-enkephalin were studied in the guinea-pig ileum bioassay. Results showed that these opioids not only activated the opiate receptor, but also altered the responsiveness of the ileum to subsequent applications of other opioid compounds. These specific, asymmetrical interactions may reflect long-term modulation of the opiate receptor. 10 references. (Author abstract modified)

**002967** Sastry, B. R. Dept. of Physiology, College of Medicine, University of Saskatchewan, Saskatoon, Saskatechewan, Canada S7N OWO **Gamma-aminobutyric acid and primary afferent depolarization in feline spinal cord.** Canadian Journal of Physiology and Pharmacology. 57(10):1157-1167, 1979.

The effects of iontophoretically applied GABA, (-)-nipecotic acid (NCA), 2,4-diaminobutyric acid, and pentobarbital on the thresholds for antidromic activation of single group-I muscle afferents were examined in decerebrated spinal cats. Results showed that a GABA-induced increase in the excitability of group-I afferent terminals was associated with depolarization of the afferent. Uptake of iontophoretically applied amino acid into the spinal cord tissue appeared to limit its action on the afferent terminal excitability. GABA exhibited preterminal depolarizing action on the group-I muscle afferents. Primary afferent depolarization produced by nerve stimulation was not significantly affected by NCA and bicuculline, suggesting it may be of diffuse origin. 41 references. (Author abstract modified)

**002968** Schmeling, William T.; Hosko, Michael J. Hosko: Dept. of Pharmacology, Medical College of Wisconsin, P. O. Box 26509, Milwaukee, WI 53226 **Effect of delta9-tetrahydrocannabinol on hypothalamic thermosensitive units.** Brain Research. 187(2):431-442, 1980.

Thermosensitive anterior hypothalamic neurons were studied in cats treated with delta9-tetrahydrocannabinol (THC, 1.0 to 2.0 i.v.). THC decreased the spontaneous firing and increased the thermosensitivity (TS) of primary thermodetector units, increased the spontaneous firing and TS of heat sensitive interneurons, and decreased the spontaneous firing and TS of cold sensitive interneurons. Results are consistent with the hypothesis that the preoptic region modulates cannabinoid-induced hypothermia. 43 references. (Author abstract modified)

**002969** Schmidt, Dieter; Kupferberg, Harvey J.; Yonekawa, Wayne; Penry, J. Kiffin. Abt. f. Neurologie, Klinikum Charlottenburg, Freie Universitat Berlin, West Berlin, Germany **The development of tolerance to the anticonvulsant effect of phenobarbital in mice.** Epilepsia. 21(2):141-147, 1980.

The development of tolerance to the anticonvulsant effect of chronically administered phenobarbital was demonstrated in mice by the maximal electroshock (MES) test. Anticonvulsant activity decreased 50% over a 5 day period. Brain and plasma levels of phenobarbital measured 2 hr after a 25mg/kg dose of phenobarbital were the same between days 1 and 5, indicating that distributional or pharmacokinetic parameters were not involved. The loss of anticonvulsant activity of phenobarbital was primarily related to the drug's effect to prevent the spread of MES-induced epileptic neuronal activity. In contrast, the anticonvulsant action of phenobarbital on seizure threshold, as measured by the minimal electroshock seizure threshold test, and on the spread of epileptic discharge induced by pentylenetetrazol (PTA), as evaluated by the PTZ infusion test, remained unchanged. 11 references. (Author abstract)

**002970** Schreiber, Robert A. Dept. of Biochemistry, University of Tennessee Center for the Health Sciences, Memphis, TN 38163 **The effect of naloxone on audiogenic seizures.** Psychopharmacology. 66(2):205-206, 1979.

The hypothesis that a low dose of naloxone would transiently potentiate the severity of audiogenic seizure (AGS) was tested. AGS prone and control mice were injected with 2 or 4mg/kg naloxone hydrochloride or saline and severity of AGS measured at 5, 10, 15, 20, and 30 minutes. The severity of AGS was significantly increased in both AGS prone and control mice 5 to 10 minutes after naloxone injection. The effect dissipated by 20 minutes postinjection. The data suggest that naloxone may interact with a receptor for an endogenous peptide which influences energy flux in the brain, and may lead to a transient reduction in the immediate availability of energy in some inhibitory area of the brain. 7 references. (Author abstract modified)

**002971** Schultz, Joachim; Kleefeld, Gertrud. Pharmazeutisches Institut der Universitat Tubingen, auf der Morgenstelle 8, D-7400 Tubingen, Germany **Cyclic adenosine 3',5'-monophosphate in rat cerebral cortical slices: effects of methoxamine and clonidine.** Pharmacology. 18(3):162-167, 1979.

Methoxamine and clonidine had no effect on basal levels of cyclic AMP in incubated slices of male Sprague-Dawley rat cerebral cortical slices, but methoxamine effectively inhibited the noradrenaline stimulated formation of cyclic AMP (inhibitory constant, 12.6mcmol/1). In the presence of adenosine (100mcmol/1), methoxamine did not inhibit the activity of noradrenaline, but was able to activate alpha-adrenergic receptors leading to enhanced formation of cyclic AMP. Clonidine inhibited the effect of noradrenaline alone or in combination with adenosine on the cyclic AMP generating system, but did not enhance the activity of submaximal concentrations of the beta-adrenergic agonist isoproterenol. Results do not support the concept of adrenergic receptors that require both alpha and beta stimulation for maximal activation of adenylate cyclase. 15 references. (Author abstract modified)

**002972** Schulz, Rudiger; Wuster, Michael; Krenss, Heinz; Herz, Albert. Dept. of Neuropharmacology, Max-Planck-Institut fur Psychiatrie, Kraepelinstrasse 2, D-8000 Munich 40, Germany **Selective development of tolerance without dependence in multiple opiate receptors of mouse vas deferens.** Nature. 285(5762):242-243, 1980.

The selective development of tolerance without dependence in multiple opiate receptors of mouse as deferens is described. Isolated vas deferens of mice chronically treated with D-Ala2-D-Leu5-enkephalin (DADL) were found to be 800 fold less sensitive to this delta-receptor agonist, whereas no cross-tolerance to mu-receptor agonists was found. On the other hand, chronic exposure of mice to sufentanyl rendered their vas deferens more than 1,000 fold less sensitive to sufentanyl, but affected their sensitivity to DADL insignficantly. Apparently, such highly tolerant preparations exhibit no detectable sign of dependence

when challenged with naloxone or clonidine. These findings favor the notion that opiate tolerance and dependence dissociate in the mouse vas deferens. 18 references. (Author abstract modified)

**002973** Schulz, Rudiger; Wuster, Michael; Duka, Theodora; Herz, Albert. Dept. of Neuropharmacology, Max-Planck-Institute of Psychiatry, Kraepelinstrasse 2, D-8000 Munich 40, Germany **Acute and chronic ethanol treatment changes endorphin levels in brain and pituitary.** Psychopharmacology. 68(3)221-227, 1980.

Acute ethanol administration increased methionine-enkephalin and beta-endorphin levels in distinct areas of male Sprague-Dawley rat brain, but chronic ethanol treatment depressed levels of these opioid peptides in most brain regions examined. The beta-endorphin content of the intermediate/posterior lobe of the pituitary of rats and guinea-pigs was decreased by 70% by chronic ethanol. Ethanol withdrawal was followed by complete recovery of endorphin levels in brain and pituitary within 2 weeks. 33 references. (Author abstract modified)

**002974** Schwabe, U.; Kiffe, H.; Puchstein, C.; Trost, T. Institut fur Pharmakologie und Toxikologie, Medizinische Hochschule Hannover, Karl-Wiechert-Allee 9, D-3000 Hannover 61, Germany **Specific binding of 3H-adenosine to rat brain membranes.** Naunyn-Schmiedeberg's Archives of Pharmacology. 310(1):59-67, 1979.

The binding of 3H-adenosine to male Wistar rat brain membranes was studied, using a microcentrifugation technique. Specific binding of 3H-adenosine was rapid, reversible, saturable, and dependent on pH and temperature. Scatchard plots of equilibrium binding data were nonlinear, suggesting the existence of two different binding sites for adenosine. The dissociation constants were 1.7mcM and 13.6mcM, and the maximum binding capacities were 31 and 165pmol/mg protein. Of 10 adenosine derivatives tested for ability to compete with 3H-adenosine binding, the phosphorylated compounds 5'-adenosine monophosphate, cyclic adenosine monophosphate, and adenosine triphosphate were the most potent. The potency of several methylxanthines in competing for 3H-adenosine binding sites paralleled their pharmacological potency as adenosine antagonists. 28 references. (Author abstract modified)

**002975** Sellinger-Barnette, Mary M.; Mendels, J.; Frazer, A. Dept. of Pharmacology, University of Pennsylvania, School of Medicine, Philadelphia, PA 19104 **The effect of psychoactive drugs on beta-adrenergic receptor binding sites in rat brain.** Neuropharmacology. 19(5):447-454, 1980.

Repeated administration of tricyclic antidepressants (amitriptyline, chlorimipramine, desmethylimipramine, and nortriptyline) and monoamine oxidase inhibitors (nialamide and tranylcipromine) lowered tritiated dihydroalprenolol (3H-DHA) binding in male Sprague-Dawley rat cerebral cortex. Repeated treatment with iprindole or bupropion also diminished 3H-DHA binding. Mianserin, chlorpromazine, diazepam, L-dopa, tripelennamine and cocaine had no effect in 3H-DHA binding. The reduction in 3H-DHA binding induced by nialamide or iprindole was due to a reduction in the maximum number of beta-adrenergic binding sites. 47 references. (Author abstract modified)

**002976** Shaar, Carl J.; Clemens, James A. Lilly Research Laboratories, Eli Lilly and Co., Indianapolis, IN 46206 **The effects of opiate agonists on growth hormone and prolactin release in rats.** Federation Proceedings. 39(8):2539-2543, 1980.

The effects of opiate agonists on growth hormone and prolactin release in Sprague-Dawley adult rats were examined. All opioid receptor agonists except Leu-5-enkephalin amide significantly stimulated growth hormone and prolactin release. Naloxone and naltrexone blocked the hormone stimulatory effects of the opioids and both naloxone and naltrexone, when administered alone, reduced serum growth hormone and prolactin concentrations. The data suggest that the opiates stimulate prolactin via an interaction with catecholaminergic neurons controlling prolactin release and stimulate growth hormone via a mechanism independent of alpha-adrenergic or general catecholaminergic influence. It is concluded that the mechanism through which cholinergic agonists act to inhibit opiate agonist stimulation of growth hormone is presently unknown. 47 references. (Author abstract modified)

**002977** Shah, Nandkumar S.; May, Deborah A.; Yates, Jane D. Ensor Foundation Research Laboratory, William S. Hall Psychiatric Institute, Columbia, SC 29202 **Disposition of levo-(3H)cocaine in pregnant and nonpregnant mice.** Toxicology and Applied Pharmacology. 53(2):279-284, 1980.

The disposition of levo-(3H)cocaine in pregnant and nonpregnant mice was examined. Concentrations of cocaine were examined at 15 min and 1, 3, and 6 hours. In all tissues, peak concentrations were attained at 15 minutes. In pregnant mice, the concentrations in decreasing order were: uterus, placenta, spleen, kidney, fat, liver, lung, brain, spinal cord, heart muscle, eye, and plasma. Fetal brain and liver, in comparison with maternal organs, accumulated much smaller amounts. During the first hour, excretion of total radioactivity was higher in the urine of nonpregnant than pregnant females. It is concluded that pregnancy alters pharmacokinetics of cocaine. 12 references. (Author abstract modified)

**002978** Shibata, Shigenobu; Oishi, Ryozo; Ueki, Showa. Dept. of Pharmacology, Faculty of Pharmaceutical Sciences, Kyushu University, Fukuoka 812, Japan **Effect of desipramine on noradrenergic inhibition of amygdaloid evoked potential.** Japanese Journal of Pharmacology. 29(3):489-492, 1979.

The effect of desipramine (DMI) on noradrenergic inhibition of the potential evoked in the medial amygdala by stimulation of the olfactory bulb (OB-AME potential) was examined in male Wistar rats. DMI (2mg/kg i.p.) potentiated the inhibition of the OB-AME potential induced by intraventricular administration of noradrenaline (NA), but reduced the inhibition of the OB-AME potential seen after stimulation of the locus coeruleus (LC). The potentiation of inhibition induced by NA is probably due to the blockade of NA uptake into noradrenergic nerve terminals, but the mechanism underlying the reduction of the inhibitory effect of LC stimulation is not clear. 9 references.

**002979** Shibuya, Haruo; Gale, Karen; Pert, Candace B. Biological Psychiatry Branch, NIMH, Bethesda, MD 20205 **Supersensitivity to GABA's effect on benzodiazepine receptors develops after striatonigral lesions.** European Journal of Pharmacology. 62(2/3):243-244, 1980.

The effect of GABA on benzodiazepine binding in the rat substantia nigra (SN) was examined 4 weeks after unilateral electrolytic lesion of the striatonigral GABA containing pathways. Specific (3H)diazepam binding was 40% lower in the lesioned SN than in the intact SN. GABA increased (3H)diazepam binding in SN membranes from both sides, but the increase was two to three times higher in the lesioned SN. Results suggest that the SN GABA receptors that proliferate in response to GABA deafferentation may be functionally linked to benzodiazepine binding sites. 5 references.

**002980** Simonds, W. F.; DeGroat, W. C. Dept. of Pharmacology, Medical School, University of Pittsburgh, Pittsburgh, PA 15261 **Antagonism by picrotoxin of 5-hydroxytryptamine-induced**



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**excitation of primary afferent neurons.** Brain Research. 192(2):592-597, 1980.

The excitatory effects of 5-hydroxytryptamine (5-HT) on afferent neurons in the cat nodose ganglion and afferent axons in the carotid sinus nerve were antagonized by picrotoxin. In the nodose ganglion preparation, picrotoxin appeared to antagonize 5-HT more effectively than it antagonized GABA. It is suggested that 5-HT may have a presynaptic modulating action in the CNS that is sensitive to picrotoxin. 36 references.

**002981** Slotkin, Theodore A.; Seidler, Frederic J.; Whitmore, William L. Dept. of Pharmacology, Duke University Medical Center, Durham, NC 27710 **Precocious development of sympatho-adrenal function in rats whose mothers received methadone.** Life Sciences. 26(20):1657-1663, 1980.

The development of the ability of insulin-induced hypoglycemia to cause reflex neuronally mediated release of adrenal catecholamines was studied in rats exposed perinatally to methadone. In control rats, the response was absent at birth and developed by the first week of postnatal age. Rats whose mothers received daily injections of methadone showed precocious development of neonatal sympathoadrenal responses, an effect which reflected earlier maturation of functional sympathetic innervation of the tissue. The developmental alteration caused by methadone was apparent even in rats withdrawn from drug at birth by cross-fostering to normal mothers; the effect also did not display a critical period, in that prenatal exposure alone produced the shift as well as did continuous exposure. Accelerated maturation of sympathoadrenal function caused by methadone appeared to be independent of nutritional or bodyweight factors, and may represent a direct drug effect on the fetus or pup. 19 references. (Author abstract)

**002982** Speciale, Samuel G., Jr.; Karoum, Farouk; Wyatt, Richard Jed. Karoum: Laboratory of Clinical Psychopharmacology, Intramural(Research Program, Saint Elizabeths Hospital, Washington, DC 20032 **Different effects of amphetamine and amfonelic acid on peripheral and central catecholamine metabolism.** European Journal of Pharmacology. 62(4):297-307, 1980.

The effects of amphetamine (AMPH) and amfonelic acid (AFA) on catecholamine metabolism in Sprague-Dawley rat peripheral sympathetic ganglia and in brain were examined. Results suggest that AMPH releases amines and shuts down catecholaminergic neuronal firing, while AFA facilitates impulse-induced release and stimulates central catecholamine turnover. The stimulant effects of AMPH, AFA, and desmethylimipramine did not appear to be directly related to their influence on central catecholamines. 42 references. (Author abstract modified)

**002983** Stamler, John F.; Brody, M. J.; Phillips, M. Ian. Phillips: Dept. of Pharmacology, University of Iowa College of Medicine, Iowa City, IA 52242 **The central and peripheral effects of Captopril (SQ 14225) on the arterial pressure of the spontaneously hypertensive rat.** Brain Research. 186(2):499-503, 1980.

The effects of Captopril on arterial pressure in spontaneously hypertensive rats were examined after intracerebroventricular (i.v.t.) or intravenous (i.v.) administration. A 75mcg dose of Captopril produced a greater hypotensive response when given i.v.t. than when given i.v., indicating that Captopril acts centrally in the rat. It is suggested tht Captopril may lower mean arterial pressure in the spontaneously hypertensive rat by blocking the central angiotensin-II system. 19 references.

**002984** Stanley, Michael. City University of New York **The effect of antipsychotic drugs on regional dopamine metabolism in rat brain and the prediction of antipsychotic efficacy. (Ph.D. dissertation).** Dissertation Abstracts International. 39(12):5869-B, 1979. Ann Arbor, Univ. Microfilms No. 7913168, 219p., 1979.

The effect of a number of antipsychotic drugs on regional dopamine (DA) metabolism was investigated in rat brain. Maximal dose of haloperidol, administered chronically, caused significant decreases in DA in striatum and tuberculum olfactorium (TO) relative to that seen acutely. DA turnover was increased to the same extent following acute or chronic treatment with an ED-50 dose of haloperidol, while neither a maximal nor ED-50 dose of clozapine altered DA turnover as compared with the same doses given acutely. Differences induced in regional DA turnover by clozapine could not be ascribed to differences in drug distribution. None of four compounds active in preclinical screening and inactive clinically in treating schizophrenia produced a regionally selective response with respect to DA metabolism. Metoclopramide and sulpiride also failed to alter DA metabolism in a regionally selective manner. Examination of dose response curves was found to differentiate antipsychotic and nonantipsychotic drugs. On the basis of effects on DA turnover, it was predicted that prelapine, thiethylperazine, and metoclopromide would display antipsychotic efficacy when tested at an adequate dose range. (Journal abstract modified)

**002985** Staunton, David A.; Young, Stephen J.; Groves, Philip M. A. V. Davis Center for Behavioral Neurobiology, Salk Institute, La Jolla, CA 92037 **The effect of long-term amphetamine administration on the activity of dopaminergic neurons of the substantia nigra.** Brain Research. 188(1):107-117, 1980.

The spontaneous firing rates of neurons in the pars compacta of the substantia nigra of male Sprague-Dawley rats were not altered by pretreatment with i.p. injections of d-amphetamine or saline for 8 or 16 days. The amphetamine pretreatment also failed to alter the i.v. dose of d-amphetamine required to reduce the spontaneous firing rate of these cells by at least 50%. This threshold dose was positively correlated with the initial spontaneous firing rate of neurons from animals pretreated with saline but not d-amphetamine. No alterations were seen in the amphetamine sensitivity of these dopaminergic neurons under conditions known to produce enhanced drug effects on motor behaviors. 46 references. (Author abstract modified)

**002986** Stefanovich, V. Hoechst Aktiengesellschaft, Frankfurt am Main Werk Albert, D-6200 Wiesbaden 12, Germany **Cyclic 3′,5′-adenosine monophosphate phosphodiesterase (cAMP PDE) and cyclic 3′,5′-guanosine monophosphate phosphodiesterase (cGMP PDE) in microvessels isolated from bovine cortex.** Neurochemical Research. 4(6):681-687, 1979.

Significant cyclic 3′,5′-adenosine monophosphate phosphodiesterace (cAMP PDE) and cyclic 3′,5′-guanosine monophosphate phosphodiesterase (cGMP PDE) activity in microvessels of bovine cortex is reported. These activities are dependent on the presence of Mg2, while absence of Ca2 is virtually without effect. When both Mg2 and Ca2 are absent, phosphodiesterase (PDE) are increased relative to PDE activity in the absence of Mg2. Xanthines (caffeine, theobromine, and theophylline) were found to be better inhibitors of cAMP PDE than of cGMP PDE. Imidazole, in very high concentrations only (100M), exhibited PDE stimulatory activity at high concentrations of both substrates. Otherwise, it exhibited PDE inhibitory properties. 5 references. (Authorabstract modified)

**002987** Steinhauer, H. B.; Anhut, H.; Hertting, G. Hertting: Pharmakologisches Institut, Universitat Freiburg, Hermann-Herder-Strasse 5, D-7800 Freiburg i. Br., Germany **The synthesis of prostaglandins and thromboxane in the mouse brain in vivo: influence of drug-induced convulsions, hypoxia and the anticonvul-**

**sants trimethadione and diazepam.** Naunyn-Schmiedeberg's Archives of Pharmacology. 310(1):53-58, 1979.

The i.v. administration of convulsant doses of pentetrazole or picrotoxin induced an increase in prostaglandin-E2 (PGE2), prostaglandin-F2alpha (PGFa), and thromboxane-B2 (TXB2)-like immunoreactive material in male NMRI mouse brain tissue. The onset of these increases coincided with the appearance of clonic seizures. The anticonvulsant drugs trimethadione and diazepam reduced the convulsions and the increase in arachidonic acid metabolites induced by pentetrazole or picrotoxin. Pentetrazole, picrotoxin, and trimethadione all failed to alter cyclooxygenase activity in brain synaptosomes. The formation of PGF2a and PGE2 under hypoxic conditions was less than 10% of the amount occurring after pentetrazole-induced convulsions of the same duration. It is concluded that the seizure-induced rise of PGF2a, PGE2, and TXB2 is the result of increased CNS activity. 23 references. (Author abstract modified)

**002988** Sternberg, Debra B.; Gold, Paul E. Dept. of Psychology, 102 Gilmer Hall, University of Virginia, Charlottesville, VA 22901 **Effects of alpha- and beta-adrenergic receptor antagonists on retrograde amnesia produced by frontal cortex stimulation.** Behavioral and Neural Biology. 29(3):289-302, 1980.

The effects of adrenergic antagonists on the development of retrograde amnesia in rats were assessed. Animals were trained on either a one trial inhibitory (passive) avoidance task or a visual discriminated avoidance Y-maze. Thirty minutes prior to training animals received an injection of the beta-adrenergic antagonist propranolol (0.5mg/kg), saline, or one of the following alpha-adrenergic antagonists: phentolamine (10mg/kg), piperoxane (5mg/kg), or phenoxybenzamine (2mg/kg). Shortly after training, the animals received frontal cortex stimulations through implanted cortical screw electrodes. The results indicate that pretreatment of rats with any of these alpha and beta-adrenergic antagonists attenuates the production of retrograde amnesia. These findings add further support to the view that an adrenergic response to amnestic treatments may be a component of a restricted set of biological systems that are involved in retrograde amnesia. 49 references. (Author abstract)

**002989** Stine, S. M.; Yang, H.-Y. T.; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Inhibition of in situ metabolism of (3H)(met5)-enkephalin and potentiation of (met5)-enkephalin analgesia by captopril.** Brain Research. 188(1):295-299, 1980.

The effects of captopril, an angiotensin-I converting enzyme inhibitor, on the metabolism, level, and pharmacological action of methionine-enkephalin (ME) were studied in Sprague-Dawley rats. Results indicate that captopril inhibited an enzyme responsible for the metabolism of intracerebroventricularly administered tritiated ME. Captopril-induced analgesia at doses that inhibited the metabolism of (3H)ME and also potentiated analgesia induced by ME. Captopril did not alter endogenous levels of ME. 23 references.

**002990** Stine, Susan Marie. University of Rochester **Mechanism of action of a catecholamide seizure-inducing agent. (Ph.D. dissertation).** Dissertation Abstracts International. 40(7):3117-B, 1980. Ann Arbor, Univ. Microfilms No. 7922692, 148p., 1979.

The neurochemical correlates of the action of H13/04, a seizure inducing catecholamide, were examined. Mice of the seizure resistant inbred C 57 BL/6 strain were studied at 26 to 31 days of age, the age for maximal drug-induced audiogenic seizure susceptibility. The data presented indicate that the primary action of H13/04 is to decrease the synthesis rate of serotonin (5-HT) by competitive inhibition of tryptophan hydroxylase. The lack of any effect on noradrenaline (NA) in vitro is consistent with the hypothesis that the primary biochemical action of this drug in on 5-HT and that the action on NA in vivo is an indirect effect possibly secondary to the inhibition of 5-HT synthesis. These observations are interpreted in terms of regional biochemical differences in monoaminergic systems and functional compartmentation of monoamines. The possible role of monoamines in audiogenic seizure susceptibility is discussed in context with a model which proposes that audiogenic seizures represent an abnormal response to stress. (Journal abstract modified)

**002991** Stokes, K. Bradley; Lee, Nancy M.; Loh, Horace H. Laboratory for Preclinical Pharmacology, NIMH, St. Elizabeth's Hospital, Washington, DC 20032 **Mouse brain DNA-dependent RNA polymerases after chronic morphine treatment.** Journal of Neurochemistry. 34(5):1058-1064, 1980.

Chronic morphine pellet implantation was found to decrease the specific activity of two forms of mouse brain RNA polymerase I and to alter the requirements of Mg2 and Mn2 for the activities of RNA polymerases II and III. DNA dependent RNA polymerases were partially purified from small dense nuclei isolated from brains of naive and morphine tolerant dependent mice, and three RNA polymerases were separated on a DEAE Sephadex-A 25 column. The three fractions, referred to as peak I, peak II, and peak III, were characterized and identified as being RNA polymerases I, II, and III, respectively. Chronic morphine pellet implantation resulted in a narcotic specific, lower specific activity of RNA polymerase I, but the specific activities of RNA polymerases II and III were not affected. Chronic morphine treatment lowered the concentration of Mg2 required for optimal activity of RNA polymerase II and elevated the Mn2/Mg2 activity ratios of RNA polymerases II and III. These specific changes in RNA polymerase function in morphine tolerance and dependence may be associated with the elevated chromatin template activities, altered chromatin phosphorylation and elevated rates of cell free translation that have been reported by others. 22 references. (Author abstract modified)

**002992** Stone, Trevor W. Dept. of Physiology, St. George's Hospital Medical School, University of London, London SW17 OQT, England **Amino acids as neurotransmitters of corticofugal neurones in the rat: a comparison of glutamate and aspartate.** British Journal of Pharmacology. 67(4):545-551, 1979.

The relative sensitivities to aspartate and glutamate of neurons receiving corticofugal innervation were examined in male Porton Wistar rats, using microiontophoretic techniques. Results suggest that corticofugal neurons with an excitatory action on cells in various parts of the brain use an amino acid, probably glutamate, as a common transmitter. No significant difference could be demonstrated in the potency ratios of glutamate aspartate on monosynaptically activated cells compared with other cells. This casts doubt on the validity of determining transmitter identity on the basis of potency ratios alone, without the support of antagonist studies. 23 references. (Author abstract modified)

**002993** Strittmatter, Warren J.; Hirata, Fusao; Axelrod, Julius; Mallorga, Pierre; Tallman, John F.; Henneberry, Richard C. Laboratory of Clinical Science, NIMH, Bethesda, MD 20205 **Benzodiazepine and beta-adrenergic receptor ligands independently stimulate phospholipid methylation.** Nature. 282(5741):857-859, 1979.

The effect of benzodiazepines on phospholipid methylation was examined by incubating C6 astrocytoma cells with (Me-3H) methionine. Stimulation of a benzodiazepine receptor with antianxiety benzodiazepines, and stimulation of the beta-adrenergic

receptor with beta-agonists, increased phospholipid methylation in C6 astrocytoma cells. Furthermore simultaneous addition of benzodiazepine and beta-adrenergic agonists increased methylation in an additive manner. It is concluded that, as phospholipid methylation alters a variety of membrane functions, these observations might provide a rationale for additional studies of whether these peripheral type receptors have specific functions reported for the central type receptor. (Author abstract modified)

**002994** Suga, Steven; Wasterlain, Claude G. Epilepsy Research Laboratory, Veterans Administration Medical Center, Sepulveda, CA 91343 **Effects of neonatal seizures or anoxia on cerebellar mitotic activity in the rat.** Experimental Neurology. 67(3):573-580, 1980.

Cerebellar mitotic activity was examined in 4-day-old Wistar rats subjected to bicuculline seizures (8mcg/kg) or exposed to a 100% nitrogen atmosphere for 16 minutes. Quantitative histological studies of mediosaggital sections of the cerebellar vermis showed reduced cerebellar mitotic activity in both experimental groups, compared to paired control littermates. The reduced mitotic activity was apparent 3 days after seizures or hypoxia, but not 1 or 2 days after the metabolic insult. 16 references. (Author abstract modified)

**002995** Supavilai, Porntip; Karobath, Manfred. Karobath: Dept. of Biochemical Psychiatry, University of Vienna, Lazarettgasse 14, A-1090 Vienna, Austria **Interaction of SQ 20009 and GABA-like drugs as modulators of benzodiazepine receptor binding.** European Journal of Pharmacology. 62(2/3):229-233, 1980.

The effects of GABA related drugs and SQ-20009, a new pyrazolopyridine with anxiolytic effects in animals, on 3H-flunitrazepam binding to membranes from rat cerebellum was examined. SQ-20009 had a direct, chloride dependent stimulatory effect on benzodiazepine receptor binding, which in turn appeared to be modulated by the associated GABA receptor. SQ-20009 also enhanced the potency of GABA and muscimol in stimulating 3H-flunitrazepam binding. 9 references. (Author abstract modified)

**002996** Supavilai, Porntip; Karobath, Manfred. Karobath: Psychiatrische Universitatsklinik Wien, Lazarettgasse 14, 1090 Vienna, Austria **Heterogeneity of benzodiazepine receptors in rat cerebellum and hippocampus.** European Journal of Pharmacology. 64(1):91-93, 1980.

The affinity for 3H-flunitrazepam was higher in rat hippocampus than in cerebellum. The GABA recognition sites associated with benzodiazepine receptors in cerebellum and hippocampus also showed different apparent affinities for GABA. The effects of etazolate on binding affinity were also twice as large in cerebellum as in hippocampus. 3 references.

**002997** Szabo, Sandor. Dept. of Pathology, Peter Bent Brigham Hospital, Boston, MA **Dopamine disorder in duodenal ulceration.** Lancet. No. 8148:880-882, 1979.

The role of dopamine in the pathogenesis or etiology of duodenal ulceration was investigated. Cysteamine-induced duodenal ulcers in rats were prevented by the dopamine agonists bromocriptine, lergotrile, and apomorphine, whereas both the severity of duodenal ulcers and the mortality among cysteamine treated rats were raised by the dopamine receptor antagonist, haloperidol. Bromocriptine and lergotrile greatly reduced gastric acid output in cysteamine treated rats. A review of the literature shows a high incidence of duodenal ulcers in patients with Parkinson's disease and a low occurrence in schizophrenias. Thus, changes in peripheral and/or central dopamine concentrations and/or receptor activity may have a role in the pathogenesis of duodenal ulceration. 25 references. (Author abstract modified)

**002998** Szente, Magdolna; Pongracz, F. Dept. of Comparative Physiology, Attila Jozsef University, Kozepfasor 52, 6726 Szeged, Hungary **Aminopyridine-induced seizure activity.** Electroencephalography and Clinical Neurophysiology. 46(5):605-608, 1979.

Cat cortex was treated with 3-aminopyridine to study the relationship between seizure generation and the extracellular K and Ca2 concentrations. This application to the surface of the cortex led to the development of a tonic epileptogenic activity within 1 minute. The well known characteristics of epileptiform discharges were readily observed by simultaneous recording from both the surface and deeper layers. It is suggested that the convulsant action of 3-aminopyridine indicates that it blocks the repolarizing potassium flux of the neuronal action potentials, and, because of the prolonged depolarization, could enhance transmitter release. 15 references.

**002999** Szmigielski, A.; Guidotti, A. Dept. of Pharmacology, M.A., 120A Narutowicza St., 90-145 Lodz, Poland **Action of harmaline and diazepam on the cerebellar content of cyclic GMP and on the activities of two endogenous inhibitors of protein kinase.** Neurochemical Research. 4(2):189-199, 1979.

The effects of drugs that alter cyclic guanosine monophosphate (cGMP) content on the activity of type-1 and type-2 protein kinase inhibitors were examined in male Sprague-Dawley rat cerebellar tissue. Harmaline (10mg/kg i.v.) increased cGMP content and decreased type-2 inhibitor activity. Diazepam (2.5mg/kg i.p.) decreased cGMP in content and increased the activity of the type-2 inhibitor. No changes in the activity of the type-1 inhibitor were observed. The drug-induced shift of type-2 inhibitor was apparent even in rats pretreated with cycloheximide, indicating it was not mediated by changes in protein synthesis. Results support the hypothesis that cGMP modulates phosphorylation in cerebellum by changing the relationship between cGMP dependent protein kinase and type-2 inhibitor content. 19 references. (Author abstract modified)

**003000** Tabakoff, Boris; Black, Richard F. Research (151), V.A. West Side Medical Center, P.O. Box 8195, Chicago, IL 60680 **A high performance liquid chromatography method for measuring brain dihydroxyphenylalanine levels and dopamine synthesis rates.** Journal of Neurochemistry. 34(6):1707-1711, 1980.

A high performance liquid chromatography method by which as little as 45 pmol of dihydroxyphenylalanine (DOPA) in brain tissues can be detected, is described. DOPA was reacted with fluorescamine and was quantitated, after chromatography, by fluorescence spectroscopy. The steady-state levels of DOPA in the mouse striatum were found to be below 90 pmol/g, but the DOPA levels were rapidly increased by inhibition of aromatic amino acid decarboxylase. The method is illustrated by a study of the effects of pharmacologic agents on DOPA synthesis in mouse striatum. 8 references. (Author abstract modified)

**003001** Tabakoff, Boris; Yanai, Joseph. Dept. of Physiology and Biophysics, University of Illinois, Medical Center, Chicago, IL 60612 **Cortexolone antagonizes development of alcohol tolerance in mice.** Psychopharmacology. 64(1):123-124, 1979.

The effect of the glucocorticoid receptor blocker, cortexolone, on the development of alcohol tolerance was investigated in mice. Mice treated with cortexolone during a period of chronic ethanol feeding displayed significantly less tolerance to a challenge dose of ethanol than mice fed ethanol but not given cortexolone. Cortexolone did not alter the hypnotic effects of ethanol in animals not previously given ethanol, and no differ-

ences were found in ethanol consumption or blood ethanol levels between ethanol fed mice receiving daily injections of cortexolone and the vehicle injected controls. It is concluded that cortexolone may be interfering with a regulatory interaction between the glucocorticoids and noradrenergic and serotonergic neurons, since these aminergic systems play an important role in the development of alcohol tolerance. 8 references. (Author abstract modified)

**003002** Tache, Yvette; Pittman, Quentin; Brown, Marvin. Peptide Biology Laboratory, Salk Institute, P.O. Box 85800, San Diego, CA 92138 **Bombesin-induced poikilothermy in rats.** Brain Research. 188(2):525-530, 1980.

The effect of ambient temperature on the rectal temperature response to intraventricular injection of bombesin was studied in conscious adult male Sprague-Dawley rats. At 4 degrees C, bombesin (50ng to 1mcg) caused a marked hypothermia which was dose dependent in magnitude and duration. This hypothermia was attenuated at 24 degrees and not evident at 31 or 33 degrees. At 36 degrees, bombesin (1 to 10mcg) induced an elevation of rectal temperature. The analogs (D-Trp8) bombesin and (D-Leu13) bombesin had no significant effects on temperature. Results suggest that bombesin acts in the brain as a poikilothermic agent by disrupting thermoregulation at temperatures below or above thermoneutrality. 20 references. (Author abstract modified)

**003003** Tagliente, Thomas Michael. City University of New York **Regional effects of barbiturates on monoamine oxidase Type A and Type B activity in the mouse brain. (Ph.D. dissertation).** Dissertation Abstracts International. 39(12):6180-B, 1979. Ann Arbor, Univ. Microfilms 7913170, 88p. 1979.

The effects of pentobarbital and phenobarbital on monoamine oxidase (MAO) activity in the mouse telencephalon, diencephalon, and brainstem were determined with serotonin (5HT, MAO-A) and beta-phenylethylamine (PEA, MAO-B) substrates. Pentobarbital increased MAO-A and MAO-B activity in telencephalon and diencephalon, but inhibited it in brainstem. Phenobarbital inhibited MAO-A activity in all three areas, but increased MAO-B activity in the telencephalon and brainstem and inhibited it in the diencephalon. In caffeine pretreated mice, pentobarbital-induced MAO-A increases were antagonized. Diencephalic MAO-B and MAO-A activity, inhibited by pentobarbital, was further inhibited by caffeine pretreatment. Caffeine pretreatment had no effect on the pentobarbital-induced increase in MAO-B activity in diencephalon or brainstem. Implications are discussed in relation to possible alterations in regional brain concentrations of the substrate amines of the metabolites of the MAO A/B reaction. (Journal abstract modified)

**003004** Tang, Siu W.; Helmeste, Daiga M.; Stancer, Harvey C. Stancer: Dept. of Psychiatry, University of Toronto, 250 College Street, Toronto, Ontario, Canada M5T 1R8 **The effect of clonidine withdrawal on total 3-methoxy-4-hydroxyphenylglycol in the rat brain.** Psychopharmacology. 61(1):11-12, 1979.

The effect of clonidine withdrawal on the brain norepinephrine system was studied in the rat. Clonidine suppressed brain total 3-methoxy-4-hydroxyphenylglycol (MHPG) significantly and no tolerance to this effect was observed up to 21 days. Cessation of clonidine treatment resulted in an elevation in the level of brain total MHPG. The suitability of the clonidine withdrawal syndrome as a model of bipolar depression is discussed. 10 references. (Author abstract)

**003005** Tang, Siu W.; Seeman, Philip. Psychopharmacology Section, Clarke Institute of Psychiatry, 250 College Street, Toronto, Canada M5T 1R8 **Effect of antidepressant drugs on serotonergic and adrenergic receptors.** Naunyn-Schmiedeberg's Archives of Pharmacology. 311(3):255-261, 1980.

The effects on serotonergic and adrenergic receptors of eight tricylic antidepressants (doxepin, amitriptyline, clomipramine, imipramine, trimipramine, nortriptyline, desipramine, and protriptyline) and four nontricyclic antidepressants (mianserin, nomifensin, iprindole, and zimelidine) were examined by direct binding assays. 3H-WB-4101 served as a label for postsynaptic alpha receptors while 3H-clonidine served to label presynaptic alpha receptors in the frontal cortex of the calf. 3H-dihydroalprenolol (3H-DHA) was used to label the beta1 adrenoceptors in the calf frontal cortex and beta2 adrenoceptors in the calf cerebellar cortex. 3H-d-Lysergic acid diethylamide (3H-LSD) and 3H-serotonin (3H-5HT) were used to label the serotonergic receptors in the calf frontal cortex. Results show that at drug concentrations which occur clinically in the plasma water, most of the tertiary amine tricyclics significantly inhibited 3H-WB-4101, 3H-LSD and 3H-5HT binding. None of the antidepressants tested had any significant effect on 3H-DHA binding. The secondary amine tricyclics as a group were not potent in inhibiting the binding of all four radiolabelled ligands. The nontricyclic antidepressant mianserin was potent in inhibiting the binding of 3H-WB-4101, 3H-clonidine, 3H-LSD, and 3H-5HT. It is suggested that the differences between the effects of the antidepressants on adrenergic and serotonergic receptors may be responsible for the differences in their therapeutic efficacies and side-effects. 56 references. (Author abstract modified)

**003006** Taniguchi, Takashi; Wang, James K. T.; Spector, Sydney. Dept. of Physiological Chemistry and Pharmacology, Roche Institute of Molecular Biology, Nutley, NJ 07110 **Properties of (3H) diazepam binding to rat peritoneal mast cells.** Life Sciences. 27(2):171-178, 1980.

Benzodiazepine binding to rat peritoneal mast cells was investigated using (3H)diazepam as the radioactive probe. The specific binding of (3H)diazepam reaches equilibrium within 10 to 15 min, is saturable, and is linear with cell number. Scatchard analysis of equilibrium binding indicates the existence of only one class of binding sites. The binding of (3H)diazepman is temperature dependent, the highest amount is bound at zero degrees C, and shows a pH optimum between pH 6.8 to 7.4. The binding of (3H)diazepam is reversible with t 1/2 = 1.2 plus or minus 0.2 min. Based on the relative potency of clonazepam and Ro5-4864 in displacing the specific (3H)diazepam binding, the binding sites in the mast cell are similar to those in the peripheral tissues like lung, liver, and kidney and are differen from those in the brain. These data indicate that the mast cells have benzodiazepine binding sites which are of the peripheral type. 21 references. (Author abstract)

**003007** Tappaz, M.; Aguera, M.; Belin, M. F.; Pujol, J. F. INSERM U 171, Groupe de Neurochimie Fonctionnelle, Dept. de Medecine Experimentale, Universite Claude Bernard, F-69373 Lyon Cedex 2, France **Autoradiography of GABA in the rat hypothalamic median eminence.** Brain Research. 186(2):379-391, 1980.

Light microscopy autoradiography was used to study possible high affinity uptake sites for exogenous radiolabeled GABA and GABA analogues in the male Sprague-Dawley rat median eminence. Results indicated that cell elements capable of accumulating GABA are localized in the external cell layer of the median eminence. It is suggested that a subpopulation of GABA nerve endings may exist in the vicinity of the primary plexus capillaries. 55 references. (Author abstract modified)

**003008** Taylor, John E.; El-Fakanany, Esam; Richelson, Elliott. Dept. of Psychiatry, Mayo Foundation, Rochester, MN 55901

**Long-term regulation of muscarinic acetylcholine receptors on cultured nerve cells.** Life Sciences. 25(26):2181-2187, 1979.

The cellular responses to long-term desensitization of muscarinic receptors were studied on mouse neuroblastoma clone N1E-115 and compared to short-term regulation of these receptors. Incubation of mouse neuroblastoma cells with the muscarinic agonist carbachol resulted in a time dependent desensitization to muscarinic receptor mediated cyclic GMP formation and a decrease in the number and affinity of muscarinic receptors as measured by the binding to intact cells of the the muscarinic antagonist 3H-quinuclidinyl benzilate (QNB). The decrease in responsiveness to cylic GMP formation reached a maximum after a 15 minute exposure to 1mM carbachol (short-term desensitization), whereas changes in (3H)QNB binding became apparent only after 1 hour exposure and reached a maximum after about 12 hours (long-term densensitization). Recovery of sensitivity after short-term desensitization was rapid, suggesting that this process may involve a conformational change in the muscarinic receptor. In contrast, recovery after long-term desensitization was prolonged and could be slowed by the inhibition of protein synthesis. Results indicate that different cellular mechanisms are involved in the short-term and long-term desensitization of muscarinic receptors. Implications for neuropsychiatric disorders such as tardive dyskinesia are discussed. 16 references. (Author abstract modified)

**003009** Tayo, F. M. Dept. of Pharmacology and Therapeutics, University of Ibadan, Ibadan, Nigeria **Effects of nomifensine on the isolated vas deferens of the rat.** Archives Internationales de Pharmacodynamie et de Therapie. 240(1):94-102, 1979.

Low concentrations of antidepressant drug nomifensine enchanced the stimulant effects of dopamine (DA) and prevented the inhibitory action of pimozide on DA-induced contractions in rat isolated vas deferens. High concentrations of nomifensine blocked the effects of DA noncompetitively. Nomifensine also enhanced noradrenaline (NA)-induced contractions and reduced phentolamine-induced antagonism of NA; higher concentrations of nomifensine blocked the effects of NA noncompetitively. Guanethidine-induced supersensitivity to NA and further enhanced the potentiating effect of nomifensine. The effect of serotonin was reduced competitively by nomifensine. Desipramine produced a similar preferential enhancement of DA-induced contractions and antagonized DA at higher concentrations. Results suggest that nomifensine may act prejunctionally by inhibiting uptake of amines and postjunctionally. 14 references. (Author abstract modified)

**003010** Tewson, T. J.; Raichle, M. E.; Welch, M. J. Welch: Edward Mallinckrodt Institute of Radiology, Washington University School of Medicine, 510 South Kingshighway, St. Louis, MO 63110 **Preliminary studies with (18F)haloperidol: a radioligand for in vivo studies of the dopamine receptors.** Brain Research. 192(1):291-295, 1980.

The synthesis of (18F)haloperidol of sufficiently high specific activity to permit the mapping of dopamine receptors in vivo in humans using positron emission tomography (PET) is reported, and preliminary work with this radioligand in vivo in monkeys is described. This in vivo work in monkeys suggests that haloperidol enters brain from blood by means of carrier mediated, facilitated diffusion rather than simple diffusion. It is noted that this unexpected finding not only assumes special inportance in the interpretation of in vivo pharmacokinetic data on dopamine receptors in man or animals, but may also be important in considerations of the possible mode of action of this drug on the CNS. 12 references.

**003011** Tolbert, Lelland C.; Thomas, Thomas N.; Middaugh, Lawrence D.; Zemp, John W. Neurosciences Program, University of Alabama, Birmingham, AL 35294 **Effect of ascorbic acid on neurochemical, behavioral, and-physiological systems mediated by catecholamines.** Life Sciences. 25(26):2189-2195, 1979.

In order to study the in vivo effect of ascorbic acid on central dopamineric systems, mice were injected with pharmacological doses (2g/kg) of ascorbate, which produced a significant elevation in brain ascorbate concentration. Injecting the mice with ascorbate: 1) blocked the amphetamine-induced increase in stereotyped behavior which has been reported to be mediated by dopaminergic neural systems, 2) had no effect on the amphetamine-induced locomotor activity thought to be mediated by norepinephrine systems, and 3) attenuated apomorphine-induced hypothermia. Possible therapeutic uses for ascorbate are suggested for conditions involving functional dopamine excess, such as schizophrenia, Huntington's chorea, and tardive dyskinesia. 33 references. (Author abstract modified)

**003012** Tsang, D.; Ng, S. C. Dept. of Biochemistry, Chinese University of Hong Kong, Shatin, N.T., Hong Kong **Effect of antenatal exposure to opiates on the development of opiate receptors in rat brain.** Brain Research. 188(1):199-206, 1980.

A study of the ontogenesis of opiate receptors in Sprague-Dawley rats showed that specific binding of (3H)methionine-enkephalin varied with brain region and with age. Binding peaked at 4 days postpartum (pp) in cerebellum, and at 8 to 17 days pp in the brainstem. In the whole forebrain, the adult level was reached at 17 days pp. Administration of morphine or naloxone to female rats before and during pregnancy significantly altered the regional development of binding sites in brains of their offspring. Results indicate that the development of (3H)methionine-enkephalin binding sites in brain follows a caudal to rostral sequence and that antenatal exposure to opiates affects the development of opiate receptors in brain. 33 references. (Author abstract modified)

**003013** Tsuchiya, Toshiro; Tami, Shoji; Fukushima, Hideaki. Research Department, Pharmaceuticals Division, Sumitomo Chemical Co., Ltd., 4-2-1, Takatsukasa, Takarazuka, Hyogo 665, Japan **Analysis of the dissociation between the neocortical and hippocampal EEG activity induced by neuroleptics.** Psychopharmacology. 63(2):179-185, 1979.

The mechanisms of dissociation between the neocortical and hippocampal EEGs following neuroleptics were investigated in electrode implanted cats. Haloperidol, ID-4708, and perphenazine produced dissociation between the neocortical and hippocampal EEGs, but thioridazine and clozapine did not. Three compounds which induced EEG dissociation selectively suppressed the neocortical activation responses produced by medial hypothalamic stimulation. In contrast, two compounds which did not induce EEG dissociation suppressed the neocortical and hippocampal activation responses produced by stimulation of the medial hypothalamus and/or the midbrain reticular formation. All neuroleptics tested decreased paradoxical sleep and increased drowsiness and slow-wave sleep with spindle activity. After administration of dissociation producing neuroleptics, positive correlations between the increase of drowsiness and the appearance of EEG dissociation were observed. 15 references. (Author abstract modified)

**003014** Tuomisto, Leena; Eriksson, Lea; Fyhrquist, Frej. Dept. of Pharmacology, University of Helsinki, Siltavuorenpenger 10, SF-00170 Helsinki 17, Finland **Vasopressin release by histamine in the conscious goat.** European Journal of Pharmacology. 63(1):15-24, 1980.

Plasma levels of arginine vasopressin (AVP) in conscious goats were increased by i.v. infusion of histamine, but only at doses (300mcg and 1mg) that also decreased arterial blood pressure. When given intracerebroventricularly, smaller doses of histamine increased plasma AVP without any concomitant decrease in blood pressure. Results indicate that histamine releases vasopressin through a central mechanism and may act as a transmitter in the vasopressin releasing system. 38 references. (Author abstract modified)

**003015** Tyler, J. L.; Gordon, J. H.; Gorski, R. A. Dept. of Biological Sciences, Northwestern University, Evanston, IL 60202 **Effects of olfactory bulbectomy and estrogen on tyrosine hydroxylase and glutamic acid decarboxylase in the nigrostriatal and mesolimbic dopamine systems of adult female rats.** Pharmacology Biochemistry and Behavior. 11(5):549-552, 1979.

The effects of estradiol benzoate (EB) given to olfactory bulbectomized and sham operated rates on tyrosine hydroxylase (TH) activity in the olfactory tubercle (OT), nucleus accumbens septi, and substantia nigra (SN) were examined. It has been previously proposed that alterations in EB behavioral sensitivity (as measured by an index of sexual receptivity, lordosis responding) which also are produced by septal destruction may reflect disruptions of GABA inhibitory feedback on dopamine cell bodies in the midbrain, which may be inhibitory to lordosis. Ten bulbectomized rates and 10 sham operated rates received either EB or oil for 3 days, then were sacrificed on day 4. Subsequent assays revealed a bulbectomy dependent decrease in TH activity in the striatum, and a lesion plus EB dependent decrease in TH activity in the OT. Glutamic acid decarboxylase (GAD) activity was slightly but significantly suppressed in the ventral tegmental region in the sham ΞB group relative to the sham oil group. Rats of the bulbectomized EB group failed to exhibit decreased GAD activity. Thus, bulbectomy may result in enhanced behavioral sensitivity to EB due to disruptions in GABA/dopamine interactions, which are similar to those observed following septal destruction and which result in diminished behaviorally inhibitory dopamine tone. 28 references. (Author abstract modified)

**003016** Uchida, Yoko. Dept. of Pharmacology, Tokyo Women's Medical College, Shinjuku-ku, Tokyo 162, Japan **Effects of chlorpromazine on lipolysis in brown and white adipose tissues of cold-exposed rats.** Japanese Journal of Pharmacology. 29(4):587-596, 1979.

The effects of chlorpromazine (CPZ) on lipolysis in intercapsular brown adipose tissue (IBAT) and epididymal white adipose tissue (EWAT) were determined in tissue from male Wistar-Imamichi rats that had been exposed to cold (4 degrees C) for 1 or 30 days. Release of free fatty acids (FFA) from the EWAT of acutely exposed rats and from the IBAT of cold acclimated rats was significantly higher than in controls. CPZ suppressed the elevated lipolytic activity in IBAT of cold acclimated rats, but not in EWAT of acutely exposed animals. The concentration of dopamine and noradrenaline in IBAT and EWAT of cold acclimated rats was decreased by i.v. administration of 6-hydroxydopamine, and FFA release from IBAT was reduced to 50% of that in untreated, cold acclimated rats. CPZ produced a further decrease in lipolytic activity in the IBAT of these animals. CPZ also depressed lipolysis stimulated by the addition of noradrenaline. Results suggest that the effect of CPZ on the lipolysis in the IBAT from cold acclimated rats is mediated by a modification of sympathetic activity. 42 references. (Author abstract modified)

**003017** Ullrich, Axel; Baierl, Peter; ten Bruggencate, Gerrit. ten Bruggencate: Institute for Physiology, University of Munchen, Pettenkoferstrasse 12, D-8000 Munchen 2, Germany **Extracellular potassium in rat cerebellar cortex during acute and chronic lithium application.** Brain Research. 192(1):287-290, 1980.

the effects of low concentrations of lithium chloride (Li), both acutely and chronically applied, on the ionic microenvironment of central neurons were investigated. Data are presented which indicate that Li related changes are due to an inhibition of the Na/K pump in CNS. Liquid ion exchanger microelectrodes were used to monitor the extracellular activity of K and Li in the cerebellar cortex of urethan anesthetized rats. The inhibitory actions of lithium upon the activity of the Na/K pump were qualitatively similar upon acute and chronic applications. The relationship between Li action on the Na/K pump and its therapeutic effects is discussed. 14 references.

**003018** Uzan, Andre; Le Fur, Gerard; Malgouris, Christiane. Pharmindustrie, Groupe Pharmuka, 35, quai du Moulin de Cage, F-92231 Gennevilliers, France **Are antihistamines sedative via a blockade of brain H1 receptors?** Journal of Pharmacy and Pharmacology. 31(10):701-702, 1979.

Mequitazine, a novel phenothiazine derivative with few or no sedative side-effects, was tested for affinity for histamine H1-receptors in guinea-pig ileum and brain. Unlike the classical sedative antihistamines promethazine and chlorpheniramine, mequitazine showed greater affinity for peripheral H1-receptors than for central H1-receptors. Mequitazine and promethazine produced a similar blockade of central alpha-noradrenoceptors in rat cortex, but chlorpheniramine was ineffective. Results suggest that these sedative side-effects of antihistamines are associated with blockade of central H1-receptors rather than alpha-adrenoceptors. 20 references.

**003019** Valdes, James J.; Cameron, William R.; Evans, Selby; Gage, Fred H. Division of Toxicology, Johns Hopkins University, 615 North Wolfe St., Baltimore, MD 21205 **Regional brain morphine injections selectively attenuate aspects of septal hyperreactivity: a multivariate assessment.** Pharmacology Biochemistry and Behavior. 12(4):563-572, 1980.

Rats given either septal or sham lesions were injected with either morphine or vehicle into either the corticomedial amygdala, posterior hypothalamus, or the ventral hippocampus, and were tested for responsivity to noxious and nonnoxious stimuli. Naloxone injections were administered to determine the opiate specificity of the effects. The data were submitted to discriminant function analyses to determine which measures were most sensitive to the manipulations. Morphine's greatest effect was a site dependent attenuation of reactivity to nonnoxious stimuli. Naloxone showed site dependent antagonism of the morphine effect as well as unspecified independent effects of its own. The data suggest the mediation of the affective component of spetal hyperreactivity by opiate receptors, and a functional differentiation between naloxone sensitive and insensitive receptors. 50 references. (Author abstract modified)

**003020** Valzelli, L.; Bernasconi, S.; Coen, E.; Petkov, V. V. Section of Neuropsychopharmacology, Istituto di Ricerche Farmacologiche Milan, Italy **Effect of different psychoactive drugs on serum and brain tryptophan levels.** Neuropsychobiology 6(4):224-229, 1980.

In a series of experiments, the effects of seven categories of psychoactive drugs (psychostimulants, barbiturates, benzodiazepines, tricyclic antidepressants, phenothiazines, butyrophenones, and piracetam) and brain tryptophan levels in the mouse were studied, employing only on pharmacologically active dose. Of the categories studied, only butyrophenones and barbiturates appeared to have no effect on serum and brain tryptophan. Caffeine greatly increased brain tryptophan, while dexamphetamine increased brain and decreased serum tryptophan. Tricyclics in-

creased only brain tryptophan; and benzodiazepines increased brain tryptophan and decreased serum tryptophan, as did phenothiazines. Piracetam increased brain tryptophan without changing serum tryptophan. Further research to better clarify the possible interactions between this essential amino acid in the brain and the responsiveness of the CNS to specific drugs is recommended. 48 references. (Author abstract modified)

**003021** Van der Heyden, J. A. M.; Venema, K.; Korf, J. Dept. of Pharmacology, Philips Duphar B. V., C. J. van Houtenlaan 36, 1381 CP Weesp, The Netherlands **In vivo release of endogenous gamma-aminobutyric acid from rat striatum: effects of muscimol, oxotremorine, and morphine.** Journal of Neurochemistry. 34(6):1648-1653, 1980.

A push/pull cannula technique was used to study the in vivo release of endogenous GABA from the striatum of chloral hydrate anesthesized rats before and after administration of muscimol, oxotremorine, and morphine. GABA release was increased after addition of depolarizing amounts of potassium to the perfusion medium. Inhibition of GABA synthesis with 3-mercaptopropionic acid (MPA) or blockade of the neuronal activity with tetrodotoxin (TTX) diminished the spontaneous release of GABA. MPA, but not TTX, reduced the potassium-induced increase in GABA release. Striatal GABA release was decreased by local application of muscimol but enhanced by picrotoxin; the latter counteracted the effect of muscimol. Intrastriatally applied serotonin did not affect the rate of endogenous GABA release. Oxotremorine added to the perfusion medium slightly increased the striatal GABA release. This effect was blocked both by locally applied atropine and haloperidol. The latter two drugs did not themselves affect the rate of GABA release. This effect was not influenced by haloperidol, but was no longer observed in the presence of nalorphine, which itself did not alter GABA release. These results indicate that GABA released from the striatum is, at least in part, of neuronal origin and that the spontaneous GABA release can be affected by various neuromodulators (including GABA, enkephalins, and acetylcholine). 56 references. (Author abstract modified)

**003022** Van Vugt, Dean A.; Meites, Joseph. Dept. of Physiology, Michigan State University, East Lansing, MI 48824 **Influence of endogenous opiates on anterior pituitary function.** Federation Proceedings. 39(8):2533-2538, 1980.

The influence of endogenous opiates on anterior pituitary function in male rats is discussed. There is growing evidence that the enodgenous opioid peptides (EOP) participate in the physiological regulation of pituitary hormone secretion. Naloxone (NAL), a specific opiate antagonist, has been shown to reduce basal serum levels of prolactin (PRL) and growth hormone, and to elevate serum levels of luteinizing hormone LH and follicle stimulating hormone. Other reports have shown that NAL can inhibit the stress-induced rise in serum PRL, raise the castration-induced increase in serum LH to greater than normal castrate values, and counteract the inhibitory effects of estrogen and testosterone on LH secretion. It is concluded that opiates appear to have no direct action on the pituitary, but there is evidence that they can alter activity of hypothalamic dopamine and serotonin in modulating secretion of pituitary hormones. 58 references. (Author abstract modified)

**003023** Vellucci, Sandra V.; File, Sandra E. Dept. of Pharmacology, University College, Gower St., London WC1E 6BT, England **Chlordiazepoxide loses its anxiolytic action with long-term treatment.** Psychopharmacology. 62(1):61-65, 1979.

The biochemical and behavioral effects of acute 5, 15, and 25 days of treatment with chlordiazepoxide (CDP, 5mg/kg) were examined in the rat. After 5 days, 5-HT levels in the midbrain, hypothalamus, and cortex were significantly higher than in controls, and the level of 5-hydroxyindoleacetic acid (5-HIAA) was significantly lower (indicating reduced turnover). After 15 days, 5-HIAA levels were significantly elevated, possibly indicating that CDP was blocking 5-HIAA transport from the brain independent of the reduced turnover. After 25 days, no significant differences were noted as compared with controls. No marked changes in noradrenaline and dopamine occurred. It appears that the reduction in 5-HT turnover is linked to the anxiolytic effects of CDP. 18 references. (Author abstract modified)

**003024** Vermes, I.; Mulder, G. H.; Smelik, P. G. Dept. of Pharmacology, Free University Medical Faculty, Van der Boechorststraat 7, 1081 BT Amsterdam, The Netherlands **Opposite effects of K-induced depolarisation on endorphin/lipotropin secretion by anterior and intermediate lobes of the rat pituitary.** European Journal of Pharmacology. 63(1):89-90, 1980.

High potassium concentrations caused an increase in the secretion of beta-endorphin/beta-lipotropin from the anterior pituitary lobes (AL) and a steady decrease in secretion from the neurointermediate lobes (NIL). About 60% of the material secreted from the AL during potassium stimulation was beta-lipotropin, but about 90% of the immunoreactivity secreted by the NIL was beta-endorphin. Haloperidol and domperidone completely abolished the potassium-induced inhibition of beta-endorphin secretion by NIL, but did not alter the response to potassium in AL. Results suggest that the peptide secretion in AL is under hypothalamic neurohumoral stimulatory control, while that in NIL is under hypothalamic neuronal inhibitory control. 5 references.

**003025** Vincent, Steven R.; McGeer, Edith G. McGeer: Kinsmen Laboratory of Neurological Sciences, Dept. of Psychiatry, University of British Columbia, Vancouver, BC, Canada V6T 1W5 **Structural specificity of high affinity (3H)-glutamate uptake in striatal homogenates.** Journal of Pharmacy and Pharmacology. 31(10):703-704, 1979.

The structural specificity of high affinity glutamate uptake was studied in male Wistar rat striatal homogenates. Results showed that L-cysteinesulfinate, L-glutamate, and L-aspartate were equally effective inhibitors of L-(3H)glutamate uptake. No significant effect was observed for ibotenate, L-glutamate diethyl ester, L-glutamine, GABA, or alpha-amino adipic acid. Significant inhibition was observed with the neuroexcitants kainic acid and N-methyl aspartate. The aspartate-like drug 2-amino-3-phosphonopropionic acid was a potent uptake inhibitor, but the glutamate-like analogue 2-amino-4-phosphonobutyric acid had no effect. Results suggest that although L-glutamate and L-aspartate are substrates of comparable affinity for the high affinity uptake system, the uptake site prefers aspartate-like compounds and may have characteristics similar to the aspartate receptor. 13 references.

**003026** Von Burg, R.; Northington, F. K.; Shamoo, A. Cheveron Environmental Health Center, P.O. Box 1272, Richmond, CA 94802 **Methylmercury inhibition of rat brain muscarinic receptors.** Toxicology and Applied Pharmacology. 53(2):285-292, 1980.

The distribution of methylmercury (MeHg) in subcellular organelles of the rat brain was examined. The distribution varied slightly in relation to the in vivo or the in vitro mode of labeling with Me203HgC1. The differences may be explained by disruption of the normal diffusion path into the brain cells and the amount of MeHg that is bound along this diffusion path. When M3203Hg and (3H)QNB (Quinuclidinyl benzilate) were added directly to brain homogenates, the subcellular fractions demonstrated a molar QNB/MdNg binding ratio greater than 1:100.

This suggests that MeHg binding sites are in considerable excess over QNB binding sites and represent a relatively large sink for decreasing effective MeHg concentration. It is suggested that the early theory involving organic to inorganic Hg conversion be reexamined as a possibility for producing the selective toxicity to the central nervous system observed in cases of MeHg poisoning. 28 references. (Author abstract modified)

**003027** Vu, Van Thanh. George Washington University **Propranolol metabolism in the dog: the effects of mode of administration and drug interactions. (Ph.D. dissertation).** Dissertation Abstracts International. 41(1):154-B, 1980. Ann Arbor, Univ. Microfilms No. 8014049, 185p., 1980.

The effects of drug interactions on the in vivo metabolism of propranolol (P) in the dog were investigated, and the effect of dosing was also examined to elucidate the first pass metabolism of P. A sensitive and specific quantitative method using a computer system was developed to measure P and seven of its major metabolites in urine and in liver. Conjugated metabolites were also determined following enzyme hydrolysis of the urine. The reliability of the analytical methods was confirmed by radiolabeled experiments which showed that most of the radioactivity was exreted into urine within 48 hours following either intravenous or oral administration of 3H-propranolol in four male dogs. It was found that only chlorpromazine and phenobarbital affect presystemic metabolism of P, and a kinetic model was proposed to explain these findings. (Journal abstract modifed)

**003028** Waddington, John L.; Cross, Alan J. Division of Psychiatry, MRC Clinical Research Centre, Watford Road, Harrow HA1 3UJ, England **Which pharmacological action of baclofen matters most?** Journal of Pharmacy and Pharmacology. 31(9):652-653, 1979.

The pharmacological actions of baclofen are discussed. Animal studies have shown that baclofen has GABA mimetic actions, but is less potent and specific than GABA agonists such as muscimol. The most potent action of baclofen may be the inhibition of excitatory amino acid neurotransmitter release. Placebo controlled trials of baclofen have revealed no antipsychotic effect, and the reduced activity of glutamic acid decarboxylase reported for postmortem schizophrenic brain tissue has not been replicated. It is concluded that the low potency and duplicity of action of baclofen render it a poor tool for the study of GABA mechanisms. 16 references.

**003029** Wallis, D. I.; Nash, H. L. Dept. of Physiology, University College, Cardiff, CF1 1XL, Wales **The action of methylated derivatives of 5-hydroxytryptamine at ganglionic receptors.** Neuropharmacology. 19(5):465-472, 1980.

Changes in resting membrane potential induced by 5-hydroxytryptamine (5-HT), methylated 5-HT derivatives, and 1-1-dimethyl-4-phenyl piperazinium were recorded from the rabbit isolated superior cervical ganglion by the sucrose gap method. The effects of quipazine and hexamethonium on these responses were also determined. Results suggest that N,N-dimethyl-5-HT and N,N,N-trimethyl-5-HT have a dual action at ganglionic nicotinic and 5-HT receptors. Potentiation of responses mediated via one type of receptor during blockade of the other suggests that 5-HT and nicotinic receptors may be in close association in the membrane. 24 references. (Author abstract modified)

**003030** Waszczak, Barbara L.; Eng, Nancy; Walters, Judith R. Experimental Therapeutics Branch, NINCDS, 9000 Rockville Pike, Bethesda, MD 20205 **Effects of muscimol and picrotoxin on single unit activity of substantia nigra neurons.** Brain Research. 188(1):185-197, 1980.

Intravenous administration of muscimol to male Sprague-Dawley rats increased unit activity in the substantia nigra pars compacta, but inhibited firing in the nigral pars reticulata. Picrotoxin and bicuculline reversed the effects of muscimol on reticulata neurons, but not on neurons in the pars compacta. Picrotoxin caused moderate increase in the activity of pars compacta neurons, but makredly stimulated the firing of pars reticulata cells. Microinotophoretically applied GABA and muscimol inhibited the firing of cells in the pars compacta and pars reticulata, but reticulata neurons were the more sensitive to these effects. 43 references. (Author abstract modified)

**003031** Wei, E. T.; Lee, A.; Chang, J. K. School of Public Health, University of California, Berkeley, CA 94720 **Cardiovascular effects of peptides related to the enkephalins and beta-casomorphin.** Life Sciences. 26(18):1517-1522, 1980.

Cardiovascular effects of peptides related to the enkephalins and the beta-casomorphin were investigated. In the urethane anesthetized rat, intravenous injections of morphine produced a short-lasting fall in heartrate and blood pressure. The fall in heartrate (which is vagal in origin) was used to bioassay peptides related to the enkephalins and beta-casomorphin. A greater than 10% decrease in heartrate was used as a quantal index of response and the intravenous ED50 were estimated. One beta-casomorphin derivative, H-Tyr-Pro-Phe-Pro-NH2, was active at 0.32. Naloxone pretreatment blocked the bradycardia produced by the enkephalins and beta-casomorphin (1-4)-NH2. The bioassay based on heartrate may prove to be useful for the rapid detection and estimation of the in vivo pharmacological activities of new opioid peptides. 23 references. (Author abstract modified)

**003032** Welle, Stephen Leo. Northern Illinois University **Serum corticosterone, glucose, and free fatty acids in hypophagic rats. (Ph.D. dissertation).** Dissertation Abstracts International. 39(12):6181-B, 1979. Ann Arbor, Univ. Microfilms 7912497, 104p. 1978.

Serum corticosterone, glucose, and free fatty acids (FFAs) were examined in bilateral lateral hypothalamic lesioned (LH), and 6-OHDA and 6-OHDA/pargyline treated rats. In Experiment 1, LH animals had lower evening basal corticosterone levels than ad lib (AL) or pair fed (PF) controls and lower morning glucose levels, ate less than controls after food replacements, and had below normal glucose increases after feeding. Compared to PF controls, 6-OHDA rats had lower morning basal glucose levels. Rats in the 6-OHDA/pargyline group had lower evening basal corticosterone than PF controls and had the largest decrease in corticosterone between basal and 30 minute postfeeding samples. They also ate less after food replacement, had smaller 10 minute postfeeding glucose increases than controls, and had lower morning basal glucose levels than PF controls. PF controls had lower morning FFA levels than AL controls. In Experiment 2, rats with 1 hour to eat were paired with placement in a sound attenuating chamber for the first 30 min of eating. LH animals showed higher FFA levels than other groups, and LH and 6-OHDA rats had larger increases in glucose levels than AL controls. Corticosterone decreased in all groups. In Experiment 3, 2-deoxyglucose injections increased glucose and FFA levels, and nicotinic acid injections increased glucose levels and decreased FFA levels. (Journal abstract modified)

**003033** Westerink, Ben H. C.; Dijkstra, Durk; Feenstra, Matthijs G. P.; Grol, Cor J.; Horn, Alan S.; Rollema, Hans; Wirix, Els. Dept. of Pharmacy, University of Groningen, Antonius Deusinglaan 2, 9713 AW Groningen, The Netherlands **Dopaminergic prodrugs: brain concentrations and neurochemical effects of**

**5,6- and 6,7-ADTN after administration as dibenzoyl esters.** European Journal of Pharmacology. 61(1):7-15, 1980.

Regional levels of the dopamine agonists 2-amino-5,6-dihydroxytetralin (5,6-ADTN) and 2-amino-6,7-dihydroxytetralin (6,7-ADTN) in female Wistar rat brain were determined after i.p. administration of the parent compounds or their dibenzoyl ester derivatives (prodrugs). Results show that ADTN levels in brain were about five times higher after administration of the dibenzoyl prodrugs than after nonesterified ADTN. Concentrations of the 5,6-isomer were five to seven times higher than those of the 6,7-ADTN. The 5,6-isomer accumulated in dopamine rich parts of the brain after administration of the dibenzoyl derivative. The 6,7-ADTN appeared to be 12 to 14 times more potent than 5,6-derivative at the receptor site. These findings suggest that the active conformation of dopamine is closer to the beta-rotamer than to the alpha-rotamer. 20 references. (Author abstract modified)

**003034** White, S. R.; Neuman, R. S. Faculty of Medicine, Memorial University of Newfoundland, St. John's, Newfoundland A1B 3V6, Canada **Facilitation of spinal motoneurone excitability by 5-hydroxytryptamine and noradrenaline.** Brain Research. 188(1):119-127, 1980.

Ionotophoretically applied 5-hydroxytryptamine (5-HT) and noradrenaline (NA) produced long-lasting changes in the excitability of lumbar motoneurons in rats and cats. Neither 5-HT nor NA directly evoked motoneuron action potentials in the absence of other excitatory input. The 5-HT antagonist methergoline reduced glutamate evoked motoneuron activity and prevented the 5-HT (but not NA) facilitation of glutamate evoked activity. Results suggest that 5-HT and NA enhance the effects of excitatory inputs to spinal motoneurons by actions on separate receptors. 13 references. (Author abstract modified)

**003035** Wilcox, Richard E.; Riffee, William H.; Smith, Robert V. Dept. of Pharmacology, College of Pharmacy, University of Texas, Austin, TX 78712 **Hypothermic effects of N-n-propylnorapomorphine in mice: antagonism by neurotransmitter receptor blockers.** Psychopharmacology. 68(1):85-88, 1980.

The dopamine antagonist haloperidol inhibited hypothermia induced in male CD-1 mice by N-n-propylnorapomorphine. Phentolamine, propranolol, sotalol, atropine, cypoheptadine, and naloxone were ineffective. Results suggest that the hypothermic response may serve as a useful model of specific dopaminergic activity of aporphines. 17 references. (Author abstract modified)

**003036** Wilder, M. Byron; OBrien, James H. Dept., of Medical Psychology, University of Oregon Health Sciences Center, Portland, OR 97201 **Evoked potential conditioning using morphine as the unconditioned stimulus in rats.** Experimental Neurology. 67(3):539-553, 1980.

Evoked potentials were recorded from four regions of male albino rat brain during a differential classical conditioning procedure in which morphine was used as the unconditioned stimulus. The conditioning procedure resulted in alterations in the cortical response to the stimulus associated with morphine, but not in the response to the differential stimulus. The conditioned cortical response persisted after withdrawal from morphine, but was expressed only when rats were morphine intoxicated. Thus, the conditioned neural response observed in this study does not reflect processes involved in the relapse of drug free addicts. 34 references. (Author abstract modified)

**003037** Willis, Gregory L.; Singer, George. Monash Dept. of Psychological Medicine, Prince Henry's Hospital, Melbourne, Australia **The failure of alpha-methyl-para-tyrosine to produce supersensitivity in 6-OHDA lesioned rats.** Pharmacology Biochemistry and Behavior. 12(3):371-376, 1980.

The mechanism whereby alpha-methyl-para-tyrosine (AMPT) reduces the behavioral impairments produced by lateral hypothalamic lesions in rats was investigated. Previous reports have suggested that the rapid behavioral recovery following lateral hypothalamic lesions is due to an AMPT-induced supersensitivity of catecholamine receptors. An alternative hypothesis which suggests that the reduction of monoamine accumulation by AMPT accounts for the shortened period of reduced food and water intake in lesioned rats was investigated. Eight doses of 6-hydroxydopamine were injected into the lateral hypothalamus to achieve a more specific depletion of catecholamines and to produce monoamine accumulation. The behavioral deficits displayed in animals pretreated with AMPT were not significantly different from those occurring in rats pretreated with saline. Although histochemical evaluation revealed that the levels of monoamine accumulation were unaffected by the AMPT pretreatment, there was a direct relationship between the severity of behavioral deficit and the volume and intensity of monoamine accumulation. Depletion of the nigrostriatal dopamine system was unrelated to the severity of behavioral impairment. Results indicate that postsynaptic supersensitivity to catecholamines cannot account for the return of behavior after hypothalamic damage. 20 references. (Author abstract modified)

**003038** Wong, Chak-Lam; Bentley, Geoffrey A. Dept. of Pharmacology, Monash University, Clayton, 3168, Victoria, Australia **The effects of cholinergic compounds on the development of morphine tolerance, dependence and increased naloxone potency in mice.** European Journal of Pharmacology. 61(2):99-109, 1980.

The development of morphine tolerance and physical dependence was dissociated from the increased potency of naloxone in antagonizing the antinociceptive effect of morphine in chronically treated male Swiss mice. In the abdominal constriction test, morphine tolerance was apparent after subcutaneous administration of 20mg/kg morphine three times a day for 4 days. Naloxone potency in mice that showed a low degree of morphine tolerance was similar to that observed in mice given only a single dose of morphine. Atropine inhibited and anticholinesterase drugs enhanced the development of increased naloxone potency with chronic morphine treatment, but the cholinergic compounds had no major effect on the development of morphine tolerance. Chronic treatment with cholinergic agonists reduced the development of physical dependence on morphine, and muscarinic antagonists enhanced physical dependence. 26 references. (Author abstract modified)

**003039** Wong, Chak-Lam; Roberts, Michael B.; Wai, Man-Keung. Dept. of Pharmacology, Faculty of Medicine, University of Hong Kong, 5 Sassoon Road, Hong Kong **The effect of phenobarbitone pretreatment on the narcotic antagonistic potency of naloxone in mice.** European Journal of Pharmacology. 62(2/3):219-223, 1980.

Phenobarbitone (5.0 to 20.0mg/kg) did not alter the antinociceptive effect of morphine measured 4.5 hours later in the tail flick assay, but naloxone antagonism of morphine was more pronounced in the male WHT/Ht mice pretreated with phenobarbitone than in controls. Concomitant administration of naloxone in the pretreatment regime did not alter the effect of phenobarbitone. The enhanced potency of naloxone was related to the dose of phenobarbitone; it was observable 3.0 and 4.5 hours after pretreatment, but not at 6.0 hours. 9 references. (Author abstract modified)

**003040** Wong, Kar-Lit; Tyce, Gertrude M. Dept. of Physiology and Biophysics, Mayo Clinic and Mayo Foundation, Roch-

ester, MN 55901 **Pyridoxal 5'-phosphate levels in brain after treatments which impair cerebral glucose metabolism.** Neurochemical Research. 4(6):821-826, 1979.

Pyridoxal 5'-phosphate (PLP) concentrations were measured in brains of rats to determine whether a deficiency of this coenzyme was a common feature in hepatic coma, ethanol intoxication, and in animals treated with L-dopa or with 5-hydroxytryptophan (5-HTP) alone or with inhibitors of MAO or of L-aromatic acid decarboxylase. These treatments have been shown previously to be associated with reduced conversion of glucose to amino acids in brain. Cerebral PLP concentrations were reduced after some of these treatments, notably injection of ethanol, or L-dopa alone or with beta-phenylisopropylhydrazine, an inhibitor of MAO, or of 5-HTP together with N-(beta-(chlorophenoxy)ethyl) cyclopropylamine hydrochloride, Lilly 51641, another MAO inhibitor. However, in other circumstances where inhibition of conversion of glucose to amino acids has been shown (treatment with 5-HTP, or with Lilly 51641, or with (N-(D,L-seryl)-N'-2,3,4-trihydroxybenzyl) hydrazine, an inhibitor of L-aromatic amino acid decarboxylase, together with L-dopa or with 5-HTP, PLP levels in brain were unchanged, or were increased (in hepatectomized rats). 21 references. (Author abstract)

**003041** Wong, Kar-Lit; Tyce, Gertrude M. Mayo Clinic, Rochester, MN 55901 **Effect of administration of 5-hydroxytryptophan and an inhibitor of L-aromatic amino acid decarboxylase on glucose metabolism in rat brain.** Neurochemical Research. 4(2):277-287, 1979.

The effect of 5-hydroxytryptophan (5-HTP) and the L-aromatic amino acid decarboxylase inhibitor N-(DL-seryl)-N'-(2,3,4-trihydroxybenzyl) hydrazine (Ro4-4602) on brain glucose metabolism was examined. Labeled glucose was injected intravenously into male Sprague-Dawley rats pretreated with 50mg/kg i.p. Ro4-4602 alone or in combination with 30mg/kg i.v. 5-HTP. The combined pretreatment with Ro4-4602 and 5-HTP increased the concentrations of 5-hydroxytryptamine (5-HT) and 5-HTP; the increase of 5-HTP was more prolonged and pronounced than that of 5-HT suggesting that Ro4-4602 slightly inhibited the brain decarboxylation reaction. After Ro4-4602 alone or combined with 5-HTP, glucose concentration was markedly increased in brain but not in plasma; the flux of 14C from labeled glucose to amino acids in brain was reduced, but brain amino acid concentrations were not altered. 32 references. (Author abstract modified)

**003042** Wong, P. T-H.; Prince, A. K. Dept. of Pharmacology, University of London, King's College, Strand, London, WC2R 2LS, England **The membrane binding of choline acetyltransferase: uptake and acetylation of (3H)-choline in rabbit cortical slices.** Neuropharmacology. 18(5):511-513, 1979.

The metabolism of tritiated choline in rabbit cortical slices was compared to that in rat brain to clarify the relationship between the molecular properties of choline acetyltransferase (ChAT), the affinity of the enzyme for membrane fragments, and its disposition in vivo. Acetylation was as efficient in rabbit as in rat cortical slices, even though rabbit ChAT lacks the net positive charge thought to localize a critical fraction of rat ChAT at the nerve terminal membrane and to mediate the efficient acetylation of incoming choline. It is suggested that binding of ChAT to synaptosomal membranes may be a better criterion of localization in vivo than net charge. Asymmetric charge distribution or hydrophilicity may explain the disposition of rabbit brain ChAT. 13 references. (Author abstract modified)

**003043** Woolf, Clifford J. Dept. of Physiology, Windeyer Building, Middlesex Hospital Medical School, Cleveland Street, London W1P 6DB, England **Intracerebral naloxone and the reaction to thermal noxious stimulation in the rat.** Brain Research. 190(2):578-583, 1980.

The effects of systemic, intracerebral and intrathecal injections of naloxone on the nervous system of 86 Sprague-Dawley rats were examined. The hot water tail immersion test was used to provide a standardized controlled noxious stimulus. Most of the rats failed to exhibit any obvious disturbance of their behavior with the i.c.v. naloxone, although some showed an increased vocalization and agitation following tail immersion. It is concluded that this study failed to provide an evidence for a tonic opioid/peptide pain controlling system in the nucleus raphe magnus of the medulla or the periaqueductal gray of the midbrain of the rat. 23 references.

**003044** Wuerthele, Suzanne Marie. Michigan State University **Regulation of nigro-striatal dopaminergic neuronal activity. (Ph.D. dissertation).** Dissertation Abstracts International. 40(9):4256-B, 1980. Ann Arbor, Univ. Microfilms No. 8006212, 140p., 1979.

Regulation of nigrostriatal dopaminergic neuronal activity was investigated via measurement of neuronal activity following systemic or intracranial administration of dopamine agonists and antagonists. Systemic administration of dopamine antagonists (haloperidol, thioridazine, clozapine, sulpiride) increased, and agonists (apomorphine, piribedil) decreased striatal concentrations of dihydroxyphenylacetic acid (DOPAC), the major acid metabolite of dopamine. Results indicate that dopamine agonists and antagonists do not influence nigro striatal neuronal activity primarily by actions postsynaptic to nigro striatal neurons. Striatal rather than nigral presynaptic mechanisms appear to be more important for this function. (Journal abstract modified)

**003045** Wulff, V. J.; Fahy, J. L. Masonic Medical Research Laboratory, Utica, NY 13503 **Effect of chlorobutanol in Limulus ventral photoreceptor latency: a model of a two component latent period.** Brain Research Bulletin. 4(6):803-807, 1979.

A model of a two component latent period, which encompasses the finding that chlorobutanol (1,1,1-trichlor-2-methyl-2-propanol) decreases the duration of the latent period of Limulus (horseshoe crab) ventral eye receptor potentials, is presented. The effect of chlorobutanol on Limulus is both concentration and intensity dependent. Between 0.05 and 1mM chlorobutanol in sea water, the extent of latency shortening approximates a linear function of the logarithm of the chlorobutanol concentration. The latency shortening effect of chlorobutanol diminishes with decreasing intensity of stimulation and virtually disappears at intensities just exceeding threshold. These results are explained by postulating that the latent period is composed of two processes only one of which is sensitive to chlorobutanol and, further, that the duration of the chlorobutanol sensitive process is not appreciably affected by the stimulating intensity. This model of a two component latent period may be tested experimentally. In several experiments, prolonged exposure of ventral photoreceptor cells to chlorobutanol coupled with a short exposure to calcium deficient sea water produced a collapse of the receptor potential followed by a slow recovery after returning to perfusion with normal sea water. During the recovery, a slow, low amplitude positive wave exists which has been tentatively called a prepotential. 12 references. (Author abstract modified)

**003046** Wyllie, M. G.; Gilbert, J. C. Pharmacology Section, Dept. of Pharmacy, Heriot-Watt University, 79 Grassmarket, Edinburgh **An investigation into the roles of synaptic vesicular Mg-ATPase in neurotransmitter release, using benzhydryl piperazines.** Archives Internationales de Pharmacodynamie et de Therapie. 241(1):4-15, 1979.

A series of benzhydryl piperazines inhibited magnesium activated adenosine triphosphatase (Mg-ATPase) in male Sprague-Dawley rat brain synaptic vesicles. These compounds also increased basal and evoked release of noradrenaline from synaptosomes. In general, noradrenaline release increased as the degree of Mg-ATPase inhibition increased. The role of Mg-ATPase in noradrenaline release is discussed. 6 references. (Author abstract modified)

**003047** Yaksh, Tony L.; Elde, Robert P. Medical Sciences Building, Mayo Clinic, Rochester, MN 55901 **Release of methionine-enkephalin immunoreactivity from the rat spinal cord in vivo.** European Journal of Pharmacology. 63(4):359-362, 1980.

The release of methionine-ekephalin immunoreactivity (MEI) from the spinal cord of the intact male Sprague-Dawley rat was studied. Basal levels of release were around 0.4ng/ml/10 minutes. Addition of 40mM potassium to the perfusate yielded a threefold increase in the levels of MEI. This increase was blocked by substitution of cobalt for calcium in the superfusate. Results suggest that MEI is stored in a releasable fraction in the cord and may act as a neurotransmitter. 11 references. (Author abstract modified)

**003048** Yeoman, R. R.; Moreno, L.; Rigor, B. M.; Dafny, N. Dafny: University of Texas Medical School, Houston, TX 77025 **Enflurane effects on acoustic and photic evoked responses.** Neuropharmacology. 19(5):481-489, 1980.

The effects of incremental doses of enflurane on sensory evoked responses in the sensory cortex, mesencephalic reticular formation, inferior colliculus, and lateral geniculate body were studied in male Sprague-Dawley rats. The amplitude of the sensory evoked responses was depressed by low doses and augmented by high doses of enflurane. The drug level at which amplitude reversal occurred was close to the threshold level for drug-induced analgesia. These effects were best observed with acoustic evoked responses. 30 references. (Author abstract modified)

**003049** Yeung, Joseph Ching-Hoi. University of Wisconsin-Madison **Contributions of and interactions between spinal and supraspinal narcotic-sensitive sites to the analgetic effect of systemically administered morphine. (Ph.D. dissertation).** Dissertation Abstracts International. 40(9):4257-B, 1980. Ann Arbor, Univ. Microfilms No. 8001652, 141p., 1979.

The contribution of supraspinal narcotic sensitive sites to the analgesic action of systemically administered morphine and the mode of interaction between narcotic agonisms exerted at the spinal and supraspinal narcotic sensitive loci in the production of analgesia were investigated in rats. Results of two studies indicate that narcotic agonism at both the spinal and supraspinal narcotic sensitive sites is essential to the production of analgesia occasioned by systemically administered morphine. Thus, neither site can be considered the primary site of narcotic action. At most doses of morphine, analgesia is a result of a multiplicative interaction of narcotic agonisms exerted at the two action sites. At unusually high morphine doses, each substrate is capable of independent action. (Journal abstract modified)

**003050** Young, W. Scott, III.; Kuhar, Michael J. Kuhar: Dept. of Pharmacology, Johns Hopkins University School of Medicine, 725 North Wolfe St., Baltimore, MD 21205 **Serotonin receptor localization in rat brain by light microscopic autoradiography.** European Journal of Pharmacology. 62(2/3):237-239, 1980.

A light microscopic autoradiographic technique was used to study the distribution of lysergic acid diethylamide (LSD) and serotonin (5-HT) receptor binding in rat brain. The 5-HT receptors showed heterogeneous distribution throughout the CNS, with particularly high levels in the dentate gyrus, parts of the hippocampal formation, nucleus parolivaris superior, superior coliculus, median raphe, spinal substantia gelatinosa, choroid plexus, subiculum, and dorsal raphe. The binding of 3H-LSD paralleled that of 3H-5-HT in all areas. 5 references.

**003051** Yutrzenka, Gerald John. University of North Dakota **Central nervous system catecholamine mediation of the anticonvulsant activity of the benzodiazepines.** Dissertation Abstracts International. 40(12):5565-B, 1980. Ann Arbor, Univ. Microfilms No. 8009788, 188p., 1979.

CNS catecholamine mediation of the anticonvulsant activity of the benzodiazepines was investigated via pretreatment of rats with agents known to specifically modify the functional activity of catecholamine neurotransmitters and observation of the anticonvulsant effects of benzodiazepines on pentylenetetrazol-induced seizures. Results indicate a role for catecholamines in the anticonvulsant activity of the benzodiazepine. A decrease in functional activity of noradrenergic neurons, accomplished by synthesis inhibition, storage depletion, or receptor blockade, was found to enhance the anticonvulsant activity. An increase in dopaminergic activity, presumably following L-dopa administration, also increased the anticonvulsive activity of the benzodiazepines. Thus, noradrenergic activity may act to attenuate, while dopaminergic activity may facilitate the full expression of the benzodiazepines in the CNS. The ration of adrenergic to dopaminergic neuronal activity may ultimately function to influence the final expression of the pharmacological properties of the benzodiazepines. (Journal abstract modified)

**003052** Zemlan, Frank P.; Corrigan, Sheila A.; Pfaff, Donald W. Dept. of Pharmacology G3, University of Pennsylvania School of Medicine, Philadelphia, PA 19104 **Noradrenergic and serotonergic mediation of spinal analgesia mechanisms.** European Journal of Pharmacology. 61(2):111-124, 1980.

The effects of alpha-adrenergic and serotonergic receptor agonists on spinal analgesia mechanisms were examined in female Sprague-Dawley rats 6 hours to 3 weeks after spinal transection. The alpha-adrenergic agonists clonidine and xylazine induced analgesia at all times after transection; this analgesia was blocked by pretreatment with the alpha-adrenergic blocker phenoxybenzamine, but not by the serotonergic blocker metergoline. The serotonergic receptor stimulants quipazine and 5-methoxy-N,N-dimethyltryptamine induced analgesia only during the first few post operative days; their effects were blocked by pretreatment with metergoline but not by phenoxybenzamine. 88 references. (Author abstract modified)

**003053** Zukin, R. Suzanne; Gintzler, Alan R. Dept. of Biochemistry, Albert Einstein College of Medicine, 1300 Morris Park Avenue, Bronx, NY 10461 **Guanyl nucleotide interactions with opiate receptors in guinea pig brain and ileum.** Brain Research. 186(2):486-491, 1980.

The effects of guanosine triphosphate (GTP) on opiate receptor steady-state binding in guinea-pig brain and ileum were examined. Results showed that low concentrations of GTP (0.2mcM) produced a modest increase in the steady-state binding of dihydromorphine, while high concentrations (10 to 50mcM) decreased the steady-state binding of dibydromorphine to opiate receptors in brain and ileum. The binding of dihydromorphine to brain homogenates was more sensitive to the inhibitory effects of GTP than was the binding of the peptide agonist D-A1a2-Met5-enkephainamide. 19 references.

## 04 MECHANISM OF ACTION: BEHAVIORAL

**003054** Ahlenius, Sven; Larsson, Knut; Svensson, Lannart. Larsson: Dept. of Psychology, University of Goteborg, Box 14158, S-400 20 Goteborg, Sweden **Stimulating effects of lisuride on masculine sexual behavior of rats.** European Journal of Pharmacology. 64(1):47-51, 1980.

Lisuride caused selective changes in the mating pattern of sexually experienced, adult male Wistar rats. The ergot derivative produced a dose dependent decrease in the number of intromissions preceding ejaculation and in ejaculatory latency, without significantly altering other components of mating behavior. Castrated, sexually inexperienced rats treated with lisuride displayed a dose dependent increase in complete heterosexual behavior. 22 references. (Author abstract modified)

**003055** Ahlenius, Sven; Larsson, Knut; Svensson, Lennart. Dept. of Pharmacology, University of Goteborg, Box 33031, S-400 33 Goteborg, Sweden **Further evidence for an inhibitory role of central 5-HT in male rat sexual behavior.** Psychopharmacology. 68(3):217-220, 1980.

The 5-hydroxytryptamine (5-HT) reuptake inhibitors zimelidine (10mg/kg i.p.) and alaproclate (20mg/kg i.p.) prolonged the ejaculation latency and postejaculatory interval in male Wistar rats treated with a subthreshold dose of 5-hydroxytryptophan (5-HTP, 12.5mg/kg i.p.). The prolongation of ejaculatory latency induced by a 50mg/kg dose of 5-HTP was antagonized by the 5-HT receptor blocking agent metergoline (1mg/kg i.p.). Results indicate that central 5-HT plays an inhibitory role in male rat sexual behavior. 26 references. (Author abstract modified)

**003056** Albert, D. J. Psychology Dept., University of British Columbia, Vancouver, British Columbia, Canada V6T 1W5 **Suppression of mouse killing by lateral hypothalamic infusion of atropine sulfate in the rat: a general behavioral suppression.** Pharmacology Biochemistry and Behavior. 12(5):681-684, 1980.

The role of cholinergic neurons in muricidal behavior induced in male hooded rats by food deprivation was examined. Bilateral injections of 3mcl lidocaine into the lateral hypothalamus blocked mouse killing in 12 of 15 animals. Atropine sulfate significantly suppressed mouse killing at a dose of 15mcg, which also suppressed food intake, but not at 1.8 or 6.0mcg. Results suggest that atropine, a cholinergic antagonist, produced a nonspecific suppression of behavior rather than a specific suppression of mousekilling. 21 references. (Author abstract modified)

**003057** Alkana, R. L.; Parker, E. S. School of Pharmacy, University of Southern California, 1985 Zonal Avenue, Los Angeles, CA 90033 **Memory facilitation by post-training injection of ethanol.** Psychopharmacology. 66(2):117-119, 1979.

The possibility that posttraining ethanol administration facilitates memory was investigated. Immediate posttraining injection of ethanol (0.75 to 4.5g/kg) significantly enhanced retention of a one trial passive-avoidance task in mice compared to saline controls. The facilitation seen at 3.0g/kg was particularly interesting since the same dose injected 10 minutes prior to training in mice induced virtually total amnesia on a similar task without altering escape latencies. The injection of ethanol in the absence of training footshock did not alter retention latencies indicating that ethanol did not enhance retention by acting as an aversive training stimulus. It is suggested that the memory facilitation may reflect ethanol's effects on neurotransmitter, macromolecular, or hormonal systems, or a reduction in interference. 25 references. (Author abstract modified)

**003058** Anderson-Baker, W. C.; McLaughlin, C. L.; **Baile, C. A.** University of Pennsylvania, School of Veterinary Medicine, New Bolton Center, Kennett Square, PA 19348 **Oral and hypothalamic injections of barbiturates, benzodiazepines and cannabinoids and food intake in rats.** Pharmacology Biochemistry and Behavior. 11(5):487-491, 1979.

To evaluate and compare CNS sites of action of chemicals which stimulate feeding, food intakes in rates were measured after ventromedial hypothalamic (VMH), lateral hypothalamic (LH), and intragastric administration. Agents administered were pentobarbital sodium (PBS), diazepam (D), and the d-isomers and l-isomers of delta9-tetrahydrocannabinol (THC). The results suggest that the VMH mediates the action of both PBS and D, but the increased feeding caused by systemic l-THC is not duplicated by VMH administration, thereby indicating an alternate site of action. It is concluded that pharmacological agents known to influence feeding when administered peripherally have localized effects on brain feeding centers that are consistent with the widely accepted model of LH and VMH function. 39 references. (Author abstract modified)

**003059** Anderson, J.; Sharman, D. F.; Stephens, D. B. School of Biology, University of Bath, Bath, England **An effect of haloperidol on the increased food and water intake induced in rabbits by 2-deoxy-D-glucose.** British Journal of Pharmacology. 66(1):5-6, 1979.

Female New Zealand rabbits treated with 300mg/kg 2-deozy-D-glucose (2DG) showed an increase in food and water intake. Pretreatment with 1mg/kg haloperidol abolished the increase in water intake, but did not prevent the increase in food intake. Results suggest that the effects of 2DG on food and water intake are mediated by separate mechanisms and that central dopaminergic neurons are involved in the control of thirst. 9 references. (Author abstract modified)

**003060** Anlezark, Gillian; Horton, Roger; Meldrum, Brian. Meldram: Dept. of Neurology, Institute of Psychiatry, de Crespigny Park, London, SE5 8AF, England **The anticonvulsant action of the (-)- and ()-enantiomers of propranolol.** Journal of Pharmacy and Pharmacology. 31(7):482-483, 1979.

The effects of (-)-propranolol and ()-propranolol on seizures induced in DBA/2 mice by loud auditory stimulation were compared. A 16mg/kg i.p. dose of (-)-propranolol provided significant protection against the tonic phase of the seizure response. This dose of ()-propranolol did not protect against seizures, but a 32mg/kg dose prevented the tonic and respiratory arrest phases of the audiogenic seizure. The greater apparent potency of (-)-propranolol may reflect more rapid entry in brain. These findings suggest that the anticonvulsant actions of propranolol are due to its membrane stabilizing effects rather than to actions on beta-adrenergic or serotonergic receptors. 17 references.

**003061** Arnt, J.; Scheel-Kruger, J. Dept. of Pharmacology and Toxicology, H. Lundbeck & Co A/S 7-9 Otiliavej, DK-2500 Copenhagen Valby, Denmark **Behavioral differences induced by muscimol selectively injected into pars compacta and pars reticulata of substantia nigra.** Naunyn-Schmiedeberg's Archives of Pharmacology. 310(1):43-51, 1979.

Turning behavior was recorded following injection of the GABA agonist muscimol into the caudal part of the male Wistar rat substantia nigra pars compacta (SNC) or pars reticulata (SNR). Results showed that muscimol has differential effects within the SNC and SNR. Turning behavior induced by muscimol injected into the SNR was antagonized by stimulation of apomorphine sensitive dopamine receptors, but not by those activated by amphetamine or 2-amino-6,7-dihydroxy-1,2,3,4-tetrahydronaphthalene. An inhibitory effect of apomorphine was

observed following injection into several dopamine containing structures. 51 references. (Author abstract modified)

**003062** Ashton, D.; Wauquier, A. Dept. of Pharmacology, Janssen Pharmaceutica Research Laboratories, B-2340 Beerse, Belgium **Behavioral analysis of the effects of 15 anticonvulsants in the amygdaloid kindled rat.** Psychopharmacology. 65(1):7-13, 1979.

A behavioral analysis is presented of the effects of clonazepam, chlordiazepoxide (CDP), diazepam, valproate sodium, diphenylhydantoin, depamide, mesuximide, mephenytoin, acetazolamide, flunarizine, carbamazepine, primidone, phenacemide, trimethadione, and meprobamate on seizure manifestations in amygdaloid kindled rats. In the standardized test system, kindled rats were given two control stimulations; drug was then administered IP and, 30 min and 24 hr later, further stimulation was given. After each stimulation the presence or absence of ipsilateral turning, closing of the ipsilateral eye, rearing up, falling over, facial clonus, forepaw clonus, hind paw clonus, hind paw tonus, and wet shaking was assessed and the duration of forepaw clonus was measured. ID50 values for inhibition of forepaw clonus 30 min after injection of each drug are reported. The ED50 doses for inhibition of the other seizure components were significantly correlated with the ID50 value for forepaw clonus. The results suggest that the kindled rat is an appropriate and sensitive model with which to assess anticonvulsant drugs. 14 references. (Author abstract modified)

**003063** Asin, Karen E. University of Illinois-Chicago Circle, Dept. of Psychology, P. O. Box 4348, Chicago, IL 60680 **Lysine vasopressin attenuation of diethyldithiocarbamate-induced amnesia.** Pharmacology Biochemistry and Behavior. 12(3):343-346, 1980.

The effect of lysine vasopressin on diethyldithiocarbamate-induced amnesia for a step through passive avoidance task was studied in rats. It was determined that although the hormone attenuates the amnesia when it is administered prior to retrieval testing, it fails to do so when it is injected prior to training. These results are consistent with other studies demonstrating the reversal of diethyldithiocarbamate-induced amnesia by catecholamine agonists. It is speculated that memory enchancement following vasopressin stems from the activation of noradrenergic mechanisms. 40 references. (Author abstract modified)

**003064** Ator, Nancy A. Johns Hopkins University School of Medicine, Division of Behavioral Biology, 720 Rutland Ave., Rm 623, Baltimore, MD **Differential effects of chlordiazepoxide on comparable rates of responding maintained by food and shock avoidance.** Psychopharmacology. 66(3):227-231, 1979.

The effects of chlordiazepoxide (CDP) on equal rates and patterns of behavior maintained under both food reinforcement and shock avoidance schedules were compared. The effect of removing food, shock, or both in separate probe sessions was also assessed. CDP produced increases in food maintained responding at doses that decreased avoidance responding. Removing food, shock, or both did not produce differential effects. The effects of chlordiazepoxide are reported as best predicted by knowledge of maintaining conditions, under certain circumstances. 24 references. (Author abstract modified)

**003065** Ayhan, I. H.; Kaymakcalan, S.; Tulunay, F. C. Department of Pharmacology, Ankara University Medical School, Sihhiye, Ankara, Turkey **Interaction between delta9-tetrahydrocannabinol and morphine on the motor activity of mice.** Psychopharmacology. 63(2):169-172, 1979.

The effects of delta9-tetrahydrocannabinol (THC) on the locomotor activity stimulating action of morphine in mice were investigated. The pretreatment of mice by THC in doses up to 20mg/kg has been found to potentiate the morphine-induced hyperactivity in a dose dependent manner, but higher doses of THC did not produce such an action. In a second series of experiments, the dose response curve of morphine for the motor activity has been found to shift to the left by the pretreatment of mice with 10mg/kg of THC. These results show a synergism between morphine and THC and suggest that both drugs may share some common site of action. 34 references. (Author abstract )

**003066** Baker, Rodney; Melchior, Christine; Deitrich, Richard. University of Colorado School of Medicine, Dept. of Pharmacology, 4200 E. 9th Avenue, Denver, CO 80262 **The effect of halothane on mice selectively bred for differential sensitivity to alcohol.** Pharmacology Biochemistry and Behavior. Dept. of Pharmacology, University of Colorado School of Medicine,

Responses to halothane and to ethanol were studied in mice selectively bred for sensitivity (long sleep, LS) or resistance (short sleep, SS) to the anesthetic effects of ethanol. Large differences in sleep time, blood anesthetic concentrations upon awakening, and body temperature were found between the two groups after ethanol, but LS and SS mice did not differ significantly in their responses to halothane. Results indicate that ethanol and halothane act through different mechanisms. 32 references. (Author abstract modified)

**003067** Balopole, Donna C.; Hansult, Carol D.; Dorph, Douglas. 80-27, 254th Street, Floral Park, NY 11004 **Effect of cocaine on food intake in rats.** Psychopharmacology. 64(1):121,122, 1979.

The effects of cocaine (10, 15, or 25mg/kg) on food intake was examined in rats trained to eat for a 5 hr period during the dark cycle. A significant dose/hours interaction was found, although total food intake over the 5 hr was essentially the same for all groups. Cocaine depressed food intake during the first hour only. However, experimental animals were found to have a higher food and water intake on days when hourly measurements were made as compared to days when only total intake was measured, suggesting some experimenter effects. This brief anorexic effect of cocaine is consistent with previous findings. 8 references. (Author abstract modified)

**003068** Balsara, J. J.; Jadhav, J. H.; Chandorkar, A. G. Dept. of Pharmacology, V. M. Medical College, Solapur, (Maharashtra) 413003, India **Effect of intraperitoneally administered GABA on haloperidol-induced catalepsy in the rat.** Psychopharmacology. 68(1):105-107, 1980.

Pretreatment with GABA (250 to 1000mg/kg i.p.) potentiated the cataleptogenic effect of haloperidol in male albino rats. At a dose of 2000mg/kg, GABA itself induced catalepsy. These results may be due to partial access of blood borne GABA to the CNS, leading to inhibition of nigrostriatal dopaminergic neurons involved in the functioning of the corpus striatum. 19 references. (Author abstract modified)

**003069** Balster, Robert L.; Baird, J. Bernard. Box 613, MCV Station, Richmond, VA 23298 **Effects of phencyclidine, d-amphetamine and pentobarbital on spaced responding in mice.** Pharmacology Biochemistry and Behavior. 11(6):617-623, 1979.

The effects of acute ip administration of phencyclidine (PCP), d-amphetamine (AMPH) and pentobarbital (PB) on differential reinforcement of low rate (10 seconds) responding were investigated in 10 mice reinforced with sweetened milk. The effects of PCP were highly consistent, with large response rate increases (and a corresponding shift toward shorter interresponse times) at doses of 1 and 3mg/kg. Higher doses generally decreased response rates and resulted in a bimodal interresponse time distri-

bution. The effects of AMPH were similar to PCP but less consistent. Although some of the Ss showed substantial response rate increases at doses between 0.3 and 10mg/kg, half of the Ss did not show increased response rates at any dose. The effects of AMPH on the interresponse time distribution were similar to PCP. The effects of PB were least like those of PCP. The effect in most Ss was to produce a dose related decrease in response rate and a flattening of the interresponse time distribution. Occasional small response rate increases were observed with PB. 22 references. (Author abstract modified)

**003070** Barany, Sven; Gunne, Lars-M. Psychiatric Research Center, S-750 17 Uppsala, Sweden **Pharmacological modification of experimental tardive dyskinesia.** Acta Pharmacologica et Toxicologica. 45(2):107-111, 1979.

Experimental tardive dyskinesia (TD) was induced in cebus apella monkeys by prolonged administration of haloperidol. The dyskinetic symptoms were reduced by a single intramuscular injection of dopamine receptor blockers or cholinergic drugs. Some compounds that act on the GABA system, including the GABA transaminase inhibitor amino-oxyacetic acid and some benzodiazepines, also reduced the TD symptoms, as did the serotonin precursor 5-hydroxytryptophan. Results with serotonin antagonists were equivocal. Results indicate that dopamine receptor blockage and increased GABA and cholinergic activity alleviate the symptoms of TD. 19 references. (Author abstract modified)

**003071** Baratti, Carlos M.; Huygens, Patricia; Mino, Jorge; Merlo, Alicia; Gardella, Javier. Catedra de Farmacologia Experimental, Facultdad de Farmacia y Bioquimica, UBA Junin 956, 5 piso, 1113 Buenos Aires, Argentina **Memory facilitation with posttrial injection of oxotremorine and physostigmine in mice.** Psychopharmacology. 64(1):85-88, 1979.

The effects of immediate and delayed posttrial injection of oxotremorine and physostigmine on retention of the passive avoidance response was examined in mice. Immediate posttrial injection of intraperitoneal oxotremorine (.125, .250, and .500 microMOL/kg) and equimolecular doses of physostigmine were found to facilitate retention. Injections given 10 min after training also significantly facilitated retention, but injections given 30 or 120 min after training did not affect retention. These findings suggest an action of oxotremorine and physostigmine on mechanisms involved in memory storage. The enhanced retention produced by oxotremorine and physostigmine was blocked by pretreatment with atropine (2microMol/kg, 20 min intraperitoneally). The retention was not modified by posttrial injection of metoxotremorine (.250 microMol/kg intraperitoneally) or neostigmine (.250 microMol/kg intraperitoneally), quaternary analogs of oxotremorine and physostigmine, respectively. The results suggest a central action of both cholinergic agents attributable to an activation of muscarcinic brain receptors. 27 references. (Author abstract modified)

**003072** Barghon, Roselyne; Costentin, Jean H. Costentin: UER de Medecine et de Pharmacie, Laboratoire de Pharmacodynamie et Physiologie, 49 rue du Maulevrier, F-76000 Rouen, France **Rotational behavior induced by unilateral electrical stimulations of nigro-striatal dopamine neurons: modification by low doses of apomorphine.** European Journal of Pharmacology. 64(1):39-46, 1980.

Unilateral electrical stimulation of the nigrostriatal dopamine neurons produced marked contralateral turning in male Sprague-Dawley rats. Repetitive stimulation led to a progressive increase in turning, followed by a decrease to initial values; this biphasic response was also seen in rats with lesions of the substantia nigra contralateral to the stimulated side, but the time course was somewhat altered. A low dose of apomorphine (25mcg/kg) slightly altered the time course and intensity of the response to stimulation in intact rats. In rats with lesions of the contralateral nigrostriatal pathway, low doses of apomorphine (6.25 to 50mcg/kg) markedly depressed contralateral turning, but high doses did not. 35 references. (Author abstract modified)

**003073** Barofsky, Anna-Lisa; Grier, H. Cannon; Pradhan, Tapas K. Dept. of Physiology and Biophysics, Howard University College of Medicine, Washington, DC 20059 **Evidence for regulation of water intake by median raphe serotonergic neurons.** Physiology & Behavior. 24(5):951-955, 1980.

Radiofrequency lesions of the median raphe nucleus (MR) did not alter daily water intake in female Sprague-Dawley rats, and electrolytic lesions of the MR produced only a transient polydipsia. In contrast, microinjection of 5,7-dihydroxytryptamine into the MR produced a small but nonsignificant drop in water consumption on the first day after treatment, followed by marked polydipsia that peaked on day 6 and declined on days 8 to 10. Results suggest that MR serotonergic neurons act as inhibitory regulators of water intake mechanisms. 26 references. (Author abstract modified)

**003074** Barr, Gordon A.; Gibbons, Judith L.; Bridger, Wagner H. Dept. of Psychiatry, Room G-50F, Albert Einstein College of Medicine, 1300 Morris Park Avenue, Bronx, NY 10461 **A comparison of the effects of acute and subacute administration of beta-phenylethylamine and d-amphetamine on mouse killing behavior of rats.** Pharmacology Biochemistry and Behavior. 11(4):419-422, 1979

The effects of beta-phenylethylamine (PEA) and d-amphetamine on mouse killing behavior were compared in male hooded rats. When given acutely, both drugs inhibit mouse killing in experienced killer rats in a dose dependent fashion. Physiologic tolerance was observed to d-amphetamine but not to PEA following 8 days of twice daily administration. Cross-tolerance between the two drugs was observed only when d-amphetamine was administered subacutely. 16 references. (Author abstract modified)

**003075** Bass, M. B.; Lester, D. Center of Alcohol Studies and Department of Psychology, Rutgers University, New Bruswick, NJ 08903 **Rats bred for ethanol sensitivity: impairment of swimming by ethanol and pentobarbital.** Psychopharmacology. 63(2):161-167, 1979.

Rats selectively bred for disparate degrees of ethanol-induced depression of spontaneous locomotor activity were trained on a swim task. Undrugged rats of the most affected line swam significantly faster than rats of the least affected line. Ethanol produced dose dependent increases in swim time in rats of the 13th generation. Averaged over trials, these increases were greater in least affected than in most affected rats and greater in males than in females, but there was no sex difference in peak impairment. Increases in swim time were uncorrelated with predrug performance. These findings were confirmed in younger F17 rats receiving 1.75g EtOH/kg i.p. Although the lines differed in ethanol-induced impairment, F17 males of the two lines were not differentially impaired by pentobarbital. The existence of task dependent line differences in ethanol sensitivity emphasizes the nonunitary nature of ethanol-induced behavioral depression. 23 references. (Author abstract modified)

**003076** Bell, Robert; Brown, Kenneth. School of Psychology, Ulster Polytechnic, Jordanstown, Co. Antrim, North Ireland **The effects of two indenopyridine and a benzothiazepin, on shock-induced defensive fighting in rats.** Progress in Neuro-Psychopharmacology. 3(4):399-402, 1979.

The indenopyridine, YG19-256, and the benzothiazepin, thiazesim, were tested for possible effects on shock-induced defensive fighting, shock reactivity, and locomotor activity in male Sprague-Dawley rats. High doses of YG19-256 significantly reduced aggression, but thiazesim had no significant effect. Neither compound produced consistent effects on shock reactivity or locomotor activity. 4 references. (Author abstract modified)

**003077** Bell, Robert; Brown, Kenneth. Dept. of Psychology, Queen's University of Belfast, Belfast, Northern Ireland **Shock-induced defensive fighting in the rat: evidence for cholinergic mediation in the lateral hypothalamus.** Pharmacology Biochemistry and Behavior. 12(4):487-491, 1980.

The suspected cholinergic mediation in the lateral hypothalamus of shock-induced defensive fighting in the rat was investigated. Bilateral microinjections of scopolamine into the lateral hypothalamus significantly reduced shock-induced defensive fighting, without altering jump threshold values. Further investigation of the lateral hypothalamus demonstrated: 1) that fighting increased in response to bilateral microinjections of physostigmine and carbachol, that social attraction remained unaltered following scopolamine treatment, and 3) that neither motor coordination nor motor activity was significantly affected by any of the treatments. 32 references. (Author abstract modified)

**003078** Ben-Ari, Y.; Tremblay, E.; Ottersen, O. P.; Meldrum, B. S. Laboratoire de Physiologie Nerveuse, Dept. de Neurophysiologie Appliquee, C.N.R.S. 91190, Gif-sur-Yvette, France **The role of epileptic activity in hippocampal and cerebral lesions induced by kainic acid.** Brain Research. 191(1):79-97, 1980.

Transection of the perforant path and diazepam treatment both blocked the epileptic activity induced by injection of kainic acid (KA) into the amygdala and reduced neuronal loss outside the injection site. KA injections in the bed nucleus of the stria terminalis or medial septum produced little brain damage outside the injection site, but intrastriatal KA injections caused lesions of the ipsilateral hippocampus. Intracerebroventricular injection of KA produced a complex behavioral syndrome associated with extensive neuronal loss, including bilateral necrosis of the pyriform and prepyriform cortices; diazepam reduced the extent of the damage and completely prevented the cortical damage. Systemic administration of KA induced motor and EEG seizures and extensive brain damage. Results suggest that intense epileptic activity is responsible for a large part of the remote neuronal loss or necrosis seen after focal KA injections. 60 references. (Author abstract modified)

**003079** Benesova, O. Dept. of Physiology and Pharmacology, Ke Karlovu 5, Prague 1, Czechoslovakia **Susceptibility to audiogenic seizures and to thiopental narcosis in rats selected for high and low activity and defecation rates.** Activitas Nervosa Superior. 21(1):46-47, 1979.

The susceptibility to audiogenic seizures and to thiopental narcosis of rats selected for high and low activity and defecation rates was investigated. Susceptibility to audiogenic seizures was tested by exposing four groups of animals to the sound of electric bells for 60 to 90 seconds after 60 seconds of adaptation in the cage. Susceptibility to depressive effects was investigated by checking the length of sleep time after the administration of thiopental. High activity, high defecation in open field Ss were found to be the most excitable animals in both experiments. 2 references.

**003080** Beninger, Richard J.; MacLennan, A. John; Pinel, John P. J. Dept. of Psychology, University of British Columbia, Vancouver, British Columbia, Canada V6T 1W5 **The use of conditioned defensive burying to test the effects of pimozide on associative learning.** Pharmacology Biochemistry and Behavior. 12(3):445-448, 1980.

The use of conditioned defensive burying behavior to test the effects of pimozide on associative learning is described. Rats shocked by a wire wrapped prod mounted on the wall of the experimental chamber buried the prod with available bedding material when they were tested 24 hr later. Injection of the neuroleptic, pimozide, before conditioning and again before testing disrupted this conditioned defensive burying behavior; however, a concomitant reduction in general activity suggests that this deficit in condition burying may reflect a general motor impairment instead of a learning deficit. The observation that rats conditioned under the influence of pimozide but tested 24 hr later while undrugged did not display deficits in conditioned burying confirms this view. Thus, neuroleptics appear to disrupt learned behavior by interfering with the performance of conditioned responses rather than by disrupting associative learning per se. 9 references. (Author abstract modified)

**003081** Beninger, Richard J.; Phillips, Anthony G. Dept. of Psychology, University of British Columbia, 2075 Westbrook Mall, Vancouver, British Columbia, V6T 1W5 Canada **The effect of pimozide on the establishment of conditioned reinforcement.** Psychopharmacology. 68(2):147-153, 1980

Pimozide (1.Omg/kg), a dopamine receptor blocker, prevented the establishment of conditioned reinforcement in male Wistar rats in a tone/lever task. This effect could not be attributed to state-dependend learning or drug-induced performance decrements. Results suggest a possible role for dopamine neurons in mediating the control of behavior by certain positive reinforcing stimuli. 35 references. (Author abstract modified)

**003082** Bernstein, Ilene L.; Vitiello, Michael V.; Sigmundi, Ronald A. Dept. of Psychology, NI-25, University of Washington, Seattle, WA 98195 **Effects of tumor growth on taste-aversion learning produced by antitumor drugs in the rat.** Physiological Psychology. 8(1):51-55, 1980.

A number of commonly used antitumor drugs (Cytoxan, Adriamycin, cytonsine arabionoside, and Vincristine) were evaluated in the rat for their ability to act as unconditioned stimuli (UCS) in a taste aversion conditioning paradigm. With one exception (cytosine arabinoside), drugs which induce nausea and vomiting in humans (Cytoxan and Adriamycin) produced significant saccharin aversions in rats. A drug which does not produce these symptoms (Vincristine) did not produce saccharin aversions. In later studies, the effect of a chronic disease state (tumor growth) on the acquisition of learned taste aversions was evaluated. Rats bearing moderate or advanced transplantable tumors were comparable to healthy controls in their formation of conditioned taste aversions. Therefore, the chronic malaise produce by a growing tumor neither attenuated nor accentuated the taste aversions produced by Cytosan or Adriamycin injections. Results are discussed in terms of their implications for human taste aversion learning. 16 references. (Author abstract)

**003083** Bhargava, H. N. Dept. of Pharmacognosy and Pharmacology, College of Pharmacy, University of Illinois, Chicago, IL 60612 **Modification of pharmacological and toxicological effects of acetophenazine, chlorpromazine and thioridazine in morphine-dependent mice.** Archives Internationales de Pharmacodynamie et de Therapie. 238(1):165-176, 1979.

The pharmacological and toxicological responses of acetophenazine, chlorpromazine, and thioridazine were determined in morphine dependent male Swiss-Webster mice. The median lethal doses for the three phenothiazine neuroleptics were decreased significantly in morphine dependent mice 6 hours after removal of the morphine pellet, when the maximum degree of

dependence was observed. Median lethal doses did not differ between morphine and placebo treated groups 24 or 72 hours after pellet removal. The decrease in motor activity induced by the phenothiazines was greater in the placebo group than in morphine withdrawn mice, and the hypothermic response to phenothiazines was enhanced in the morphine withdrawn group. It is concluded that the effects of phenothiazine neuroleptic drugs can be modified in narcotic dependent subjects. 21 references. (Author abstract modified)

**003084** Bhargava, Hemendra N. Dept. of Pharmacognosy and Pharmacology, College of Pharmacy, University of Illinois, Chicago, IL 60612 **Comparative effects of synthetic enkephalinamides and morphine on abstinence responses in morphine-dependent mice.** Pharmacology Biochemistry and Behavior. 12(5):645-649, 1980.

The effects of the synthetic enkephalinamides D-Ala2-Met5-enkephalinamide and D-Met2-Pro-5-enkephalinamide were compared with those of morphine on abstinence responses of morphine dependent male Swiss-Webster mice. When administered intracerebroventricularly, all three compounds reversed the naloxone precipitated jumping response; on a molar basis, D-Met2-Pro5-enkephalinamide was the most potent and morphine was the least potent. The enkephalinamides and morphine also prevented the hypothermia normally associated with morphine withdrawal. 16 references. (Author abstract modified)

**003085** Bhargava, Hemendra N. Dept. of Pharmacognosy and Pharmacology, College of Pharmacy, University of Illinois, Chicago, IL 60612 **The effects of thyrotropin-releasing hormone on the central nervous system responses to chronic morphine administration.** Psychopharmacology. 68(2):185-189, 1980.

Intracerebral administration of thyrotropin releasing hormone (TRH) to morphine dependent male Swiss-Webster mice inhibited the hypothermic response observed during abrupt or naloxone precipitated withdrawal. The naloxone precipitated withdrawal jumping response was also inhibited. A single subcutaneous (sc) injection of TRH did not modify the development of morphine dependence. Multiple sc injections of TRH prior to and during morphine pellet implantation inhibited the hypothermic withdrawal response but did not modify naloxone-induced jumping. Results suggest that separate sites may initiate jumping behavior and affect temperature regulation during morphine withdrawal. 22 references. (Author abstract modified)

**003086** Bhattacharyya, A. K.; Aulakh, C. S.; Pradhan, S.; Ghosh, P.; Pradhan, S. N. Dept. of Pharmacology, Howard University College of Medicine, Washington, DC 20059 **Modification of behavioral and neurochemical effects of cocaine by haloperidol.** Archives Internationales de Pharmacodynamie et de Therapie. 238(1):71-80, 1979.

Cocaine (20mg/kg i.p.) stimulated spontaneous motor activity and induced stereotypy in male Wistar rats. The cocaine-induced stereotypy was reduced or blocked by 0.015mg/kg i.p. haloperidol, but the drug-induced hyperactivity was blocked only when the dose of haloperidol was raised to 0.03mg/kg. Cocaine decreased the norepinephrine and serotonin contents of diencephalon/midbrain (DM) and pons-medulla and increased dopamine contents in the DM and caudate nucleus. Haloperidol also reversed these neurochemical effects of cocaine. 20 references. (Author abstract modified)

**003087** Biegon, Anat; Segal, Menahem; Samuel, David. Dept. of Isotope Research, Weizmann Institute of Science, Rehovot, Israel **Sex differences in behavioral and thermal responses to pargyline and tryptophan.** Psychopharmacology. 61(1):77-80, 1979.

The effects of parenterally injected pargyline and tryptophan on rectal temperature and behavior were studied in rats. Pargyline alone produced hypothermia and pargyline followed by low doses of tryptophan caused a behavioral syndrome consisting of tremor, hindlimb abduction, forepaw treading, and straub tail. Pargyline followed by higher doses of tryptophan produced hypothermia, a dose dependent behavioral syndrome, and mortality. The results suggest a complex role for serotonin in thermoregulation. Sex differences observed suggest higher activity of serotonin in female rat brains following the drug treatment, which may be accounted for by a higher utilization rate of tryptophan. 19 references. (Author abstract modified)

**003088** Blasig, J.; Meyer, G.; Hollt, V.; Hengstenberg, J.; Dum, J.; Herz, A. Dept. of Neuropharmacology, Max-Planck-Institut fur Psychiatrie, Kraepelinstrasse 2, D-8000 Munich 40, Germany **Non-competitive nature of the antagonistic mechanism responsible for tolerance development to opiate-induced analgesia.** Neuropharmacology. 18(5):473-481, 1979.

Dose/response curves for the analgesic effects of morphine were obtained in male Sprague-Dawley rats with different degrees of morphine tolerance. Increasing tolerance was reflected in an increasingly large shift to the right and depression of the maximum effect in the dose/response curves. When responses produced by morphine were plotted against the concentrations of the drug in the brain, no change in receptor affinity was apparent. Results suggest that the development of tolerance to morphine involves noncompetitive changes in the transduction process between receptor occupation and response, rather than qualitative changes in receptor binding sites themselves. 27 references. (Author abstract modified)

**003089** Blundell, J. E.; Latham, C. J. Biopsychology Laboratories, Psychology Dept., Leeds University, Leeds, LS2 9JT, England **Serotonergic influences on food intake: effect of 5-hydroxytryptophan on parameters of feeding behaviour in deprived and free-feeding rats.** Pharmacology Biochemistry and Behavior. 11(4):431-437, 1979.

The effects of the serotonin precursor 5-hydroxytryptophan (5-HTP) on feeding behavior were examined in food deprived and free feeding male hooded Lister rats. In food deprived rats, 5-HTP caused a dose related inhibition of food intake, which was mildly antagonized by the peripheral decarboxylase inhibitor MK-486. The inhibition of food intake by 5-HTP reflected a reduced number of eating bouts and a slower rate of eating; MK-486 did not antagonize the effect of 5-HTP on eating rate. In free feeding rats, 5-HTP caused a reduction in meal size and a slowing of the intrameal rate of eating. 50 references. (Author abstract modified)

**003090** Blundell, John E.; Latham, Colin J. Biopsychology Section, Psychology Dept., University of Leeds, Leeds, LS2 9JT, England **Characterisation of adjustments to the structure of feeding behaviour following pharmacological treatment: effects of amphetamine and fenfluramine and the antagonism produced by pimozide and methergoline.** Pharmacology Biochemistry and Behavior. 12(5):717-722, 1980.

The effects of amphetamine and fenfluramine on feeding patterns in male hooded Lister rats were studied. Amphetamine induced anorexia characterized by a long initial delay in feeding, followed by infrequent short bursts of eating. Fenfluramine markedly slowed the rate of eating. The effects of amphetamine were antagonized by the dopamine receptor blocking drug pimozide, and those of fenfluramine were aantagonized by methergoline, a serotonin receptor blocker. 27 references. (Author abstract modified)



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**003091** Bodnar, Richard J.; Zimmerman, Earl A.; Nilaver, Gajanan; Mansour, Alfred; Thomas, Lucy W.; Kelly, Dennis D.; Glusman, Murray. Dept. of Behavioral Physiology, New York State Psychiatric Institute, New York, NY **Dissociation of cold-water swim and morphine analgesia in Brattleboro rats with diabetes insipidus.** Life Sciences. 26(19):1581-1590, 1980.

The hypothesized mediation by vasopressin of the analgesic responses to morphine and cold water stress was investigated by comparing the analgesic responses of homozygous Brattleboro rats with diabetes insipidus with those of normal rats of the same strain of similar weight. Brattleboro rats exhibited hypersensitive responses to foot shock which were brought back to within normal limits by systemic administration of arginine vasopressin and desamine-D-arginine vasopressin. While Brattleboro rats failed to display an analgesic response to cold water swim stress, they displayed a normal analgesic response to morphine. These results provide further evidence for dissociation of pain inhibitory mechanisms into opioid and nonopioid components, and suggest that vasopressin might be involved in the elucidation of the latter component. 73 references. (Author abstract modified)

**003092** Boissier, J. R.; Dumont, C.; Laurent, J.; Oberlander, C. Centre de Recherches Roussel-Uclaf 111, route de Noisy, F-93230 Romainville, France **/Psychopharmacological profile of a new dopaminergic agonist, RU 24213./** Profil psychopharmacologique d'un nouvel agoniste Dopaminergique, le RU 24213. Psychopharmacology. 68(1):15-23, 1980.

The behavioral effects of RU-24213 were compared with those of apomorphine, dexamphetamine, bromocriptine, and L-dopa. In mice, RU-24213 reduced locomotor hyperactivity during exploration and subsequently stimulated activity. The drug elicited dose related stereotypies in rats and delayed the catelepsy induced by prochlorperazine. RU-24212 caused contralateral turning in animals with unilateral chemical lesions of the nigrostriatal pathway. Stereotypies and rotations induced by RU-24213 were blocked by haloperidol and decreased by alpha-methyltyrosine. Results suggest that RU-24212 stimulates dopamine receptors directly and indirectly. 25 references. (Author abstract modified)

**003093** Boren, James Leonard. State University of New York at Albany **Attenuation of tonic immobility in chickens by 5-methoxy-N,N-dimethyltryptamine and p-chloroamphetamine. (Ph.D. dissertation).** Dissertation Abstracts International. 40(12):5858-B, 1980. Ann Arbor, Univ. Microfilms No. 8013674, 90p., 1979.

The effects of several drugs which produce a serotonergic behavioral syndrome in rats on the duration and susceptibility to tonic immobility (TI) in chickens were investigated in eight experiments. A low dose 5-methoxy-N,N-dimethyltryptamine (5-MeODMT) enhanced TI durations while high doses of 5-MeODMT or p-choloroamphetamine (PCA) resulted in a significant decrease in the duration and susceptibility to TI. t-hydroxy-L-tryptophan did not affect TI duration or susceptibility. Pretreatment of animals with alpha-methyl-P-tyrosine did not affect the decrease of TI durations susceptibility produced by 5-MeODMT or PCA, suggesting that the effect of these agents on TI does not require intact stores of catecholamines. However, prior serotonin synthesis inhibition with p-chlorophenylalanine produced a partial blockade of the PCA attenuation of TI. Competing responses, in terms of enhanced locomotor activity, cannot account for the decreased TI durations after 5-MeODMT or PCA since both agents produced a decrease in open-field activity. Results are discussed in terms of a proposed dichotomy between drugs affecting presynaptic versus postsynaptic serotonergic receptors. (Journal abstract modified)

**003094** Bouyer, Jean-Jacques; Dedet, Laure; Joseph, Jean-Paul; Rougeul, Arlette. Laboratoire de Neurophysiologie comparee, Universite P. and M. Curie, 4 place Jussieu, F-75230 Paris, Cedex 05, France **Modification of spontaneous ECoG and behavior in cat by monoamine precursors.** Psychopharmacology. 65(1):49-54, 1979.

The effects of increasing the brain monoamine content on the three types of localized rhythms identified in somatic area I, mu-type rhythms, were studied in freely moving cats. Increases in brain monoamines, catecholamines and serotonin, were produced by injecting L-dopa and 5-HTP. L-tyrosine, L-tryptophan and tryptamine were also tested. It is concluded that the two subsets of rhythms, one accompanying high levels of alertness and vigilance and the other appearing during quiet wakefulness, are related to the catecholaminergic systems, while those characterizing drowsiness seem to be controlled by a serotoninergic system. The latter, however, is distinct from that controlling slow sleep. 22 references. (Author abstract)

**003095** Bouyer, Jean-Jacques,; Joseph, Jean-Paul; Rougeul, Arlette. Laboratoire de Neurophysiologie comparee, Universite P. and M. Curie, 4 place Jussieu, F-75230 Paris, Cedex 05, France **Effects of two neuroleptic drugs on focal somatoparietal rhythms in free awake cats.** Psychopharmacology. 65(1):55-58, 1979.

The effects of two neuroleptic drugs on focal somatoparietal rhythms were tested in free awake cats. Systemic administration of chlorpromazine (CPZ) and haloperidol (HP), neuroleptics which presumably block catecholamine receptors, leads to a suppression of the waking mu-type rhythms. There is clear difference, however, in that CPZ leads to slow wave sleep while HP only induces sustained drowsiness. The difference in their action is tentatively explained by their differential effect on an enzyme that is not involved in the metabolism of biogenic amines, tryptophan pyrrolase. It is suggested that it is through this pathway that CPZ might increase and HP might decrease brain tryptophan and thereby lead to opposite changes in brain 5-HT content. 19 references. (Author abstract modified)

**003096** Brands, B.; Baskerville, J. C.; Herne, R.; Hirst, M.; Gowdy, C. W. Dept. of Pharmacology, University of Western Ontario, London, Canada N6A 5C1 **Sparingly-soluble narcotic zinc tannates caused protracted analgesia in rats.** Neuropharmacology. 19(5):443-446, 1980.

Pain thresholds were determined in male Sprague-Dawley rats by the titration footshock technique for 5 to 8 days after a single subcutaneous injection of zinc tannate salts of heroin (HZT, 41.0 and 81.9mg/kg), 1-alpha-acetylmetadol (LZT, 41.0 and 81.9mg/kg), or hydromorphine (DZT, 39.9 and 79.8mg/kg). Pain threshold 24 hours after injection in a slow release vehicle were elevated for all preparations except the low dose HZT. Pain thresholds were significantly elevated for 3 days after low dose LZT, 4 days after both doses of DZT, and 5 days after high dose LZT. 13 references. (Author abstract modified)

**003097** Brands, Bruna; Baskerville, J. C.; Hirst, M.; Gowdey, C. W. Dept. of Pharmacology, University of Western Ontario, London, Ontario, Canada **Zinc tannate salts of heroin, LAAM and hydromorphone attenuate opiate withdrawal syndrome.** Psychopharmacology. 68(3):311-314, 1980.

Single injections of the zinc tannate salts of heroin, hydromorphone, or levo-alpha-acetylmethadol attenuated the codeine withdrawal syndrome in male Sprague-Dawley rats. Weight loss in animals treated with the narcotic agonists 12 hours after codeine withdrawal was significantly less than that in rats given only the slow release vehicle. Rats treated with the narcotic agonists were generally less irritable than the vehicle controls. 18 references. (Author abstract modified)

**003098** Broderick, Patricia Ann. St. John's University **Lithium and L-tryptophan synergism in muricidal behavior antagonism: central serotonergic correlates in the muricidal rat. (Ph.D. dissertation).** Dissertation Abstracts International. 41(1):149-B, 1980. Ann Arbor, Univ. Microfilms No. 8014073, 95p., 1979.

The effects of lithium and L-tryptophan on central serotonergic pathways were studied in rat muricidal (mouse killing) behavior, a model pragmatically employed to screen antidepressant drugs. Lithium and L-tryptophan, intraperitoneally, antagonized muricidal behavior, acutely and chronically, in isolated, male, Long Evans rates in a dose response fashion, with no significant neurotoxic impairment on rotarod performance. Lithium and L-tryptophan acted synergistically in muricidal behavior antagonism; this synergism was reflected peripherally in both lithium and L-tryptophan plasma levels. It is speculated that the addition of L-tryptophan to lithium regimens may reduce the potential toxicity of lithium by producing the same behavioral and biochemial effect with a lower lithium dosage regimen. (Journal abstract modified)

**003099** Brown, David R.; Blank, Michael S.; Holtzman, Stephen G. Dept. of Pharmacology, Emory University School of Medicine, Atlanta, GA 30322 **Suppression by naloxone of water intake induced by deprivation and hypertonicsaline in intact and hypophysectomized rats.** Life Sciences. 26(18):1535-1542, 1980.

The suppression by naloxone of water intake induced by deprivation and hypertonic saline in intact and hypophysectomized rats was investigated. Naloxone, an opiate antagonist, was administered to intact and hypophysectomized male rats following hypertonic saline pretreatment or 12 hour water deprivation. Water intake following hypertonic saline or water deprivation was reduced by 0.01 to 10mg/kg of naloxone in a dose related fashion in both intact and hypophysectomized rats. Water consumption induced by hypertonic saline administration appeared to be more susceptible to the suppressant effects of naloxone than did that evoked by water deprivation. These results demonstrate that naloxone reduces water intake in the rat following intracellular dehydration by hypertonic saline administration, as well as after general dehydration induced by water deprivation. Furthermore, the suppressant effects of naloxone on water intake do not appear to involve pituitary endorphins, although a possible involvement of antidiuretic hormone in these effects cannot be excluded. 53 references. (Author abstract modified)

**003100** Brown, David R.; Holtzman, Stephen G. Dept. of Pharmacology, Emory University School of Medicine, Atlanta, GA 30322 **Suppression of deprivation-induced food and water intake in rats and mice by naloxone.** Pharmacology Biochemistry and Behavior. 11(5):567-573, 1979.

The effects of naloxone, an opiate antagonist, on appetitive behavior were studied in male and female rates and male mice after periods of food or water deprivation ranging from 12 to 48 hours. Naloxone reduced postdeprivational water intake in most groups of rates and mice in a dose related manner. Naloxone suppression of water consumption appeared to be independent of sexual differences in rats, and phase of the diurnal cycle and length of the deprivation interval in both rats and mice. Postdeprivational food intake in male rates and mice was also reduced by naloxone in a dose dependent fashion. This naloxone effect was less pronounced than actions observed with water intake, and tended to diminish with lengthening food deprivation periods. In general, mice appeared to be less sensitive than rates to naloxone suppression of food and water intake. The fact that low doses of naloxone can elicit these effects suggests that the drug is acting at specific tissue sites, possibly endorphine receptors. 38 references. (Author abstract modified)

**003101** Brown, David R.; Holtzman, Stephen G. Dept. of Pharmacology, Emory University School of Medicine, Atlanta, GA 30322 **Evidence that opiate receptors mediate suppression of hypertonic saline-induced drinking in the mouse by narcotic antagonists.** Life Sciences. 26(18):1543-1550, 1980.

The effects of naloxone, its dextro-stereoisomer, and five other narcotic antagonists on water intake were studied using intraperitoneal administration of a 2M sodium chloride solution as the model for intracellular dehydration. l-Naloxone reduced drinking in the mouse in a dose dependent fashion with an ED50 of 0.55mg/kg. In contrast, d-naloxone failed to suppress water consumption at doses up to 10mg/kg. The other narcotic antagonists tested (naltrexone, diprenorphine, levallorphan, oxilorphan, and nalorphine) also produced dose dependent decreases in water consumption. The order of potency of these narcotic antagonists in suppressing water intake was highly correlated with their orders of potency in other procedures involving the opiate receptor. The stereoselectivity and order of potency suggest that the suppressant effects of the narcotic antagonists on drinking induced by hypertonic saline administration in the mouse are mediated through an opiate receptor dependent mechanism. 37 references. (Author abstract modified)

**003102** Buckett, W. R. Centre de Recherche Merrell International, 16 rue d'Ankara, F-67084 Strasbourg Cedex, France **The influence of morphine dependence on some specific effects mediated by monoaminergic and GABAergic systems.** Psychopharmacology. 66(3):233-238, 1979.

The effects of drugs modifying neurotransmitter functions were studied in rats during morphine withdrawal in comparison with controls withdrawn from saline. The sterotypy due to dopaminergic stimulation by apomorphine was significantly potentiated in the rats withdrawn from morphine. Characteristic wet dog shake behavior induced by elevating brain levels of serotonin with 5-hydroxy-DL-trytophan preceded by the decarboxylase inhibitor benserazide was similar in animals withdrawn from eithe morphine or saline. The hypothermia and the general behavior following elevation of brain GABA levels with GABA transaminase inhibitors did not differ significantly between morphine withdrawn and saline withdrawn rats. The central cholinergically mediated hypothermia and tremor induced by tremorine was similar in both groups, but the peripheral chromodacryorrhea was blocked during morphine withdrawal. It is concluded that during morphine withdrawal in the rat, the behavior mediated by dopaminergic system shows enhancement, but effects dependent upon central serotonin, GABA, and cholinergic systems are not affected. 26 references. (Author abstract modified)

**003103** Burridge, S. L.; Blundell, J. E. Dept. of Psychology, University of Leeds, Leeds, LS2 9JT, England **Amphetamine anorexia: antagonism by typical but not atypical neuroleptics.** Neuropharmacology. 18(5):453-457, 1979.

The effects of typical neuroleptics (pimozide, piflutixol, cis-z-flupenthixol, and spiroperidol) and atypical neuroleptics (thioridazine and clozapine) on amphetamine-induced anorexia in male Lister hooded rats were examined. All neuroleptics showed a dose related suppression of food intake, but were tested against amphetamine only in doses that did not themselves suppress feeding. The atypical neuroleptics failed to antagonize amphetamine-induced anorexia. The typical neuroleptics attenuated anorexia induced by 1.0 or 2.0mg/kg amphetamine, but had no effect on anorexia induced by 0.5mg/kg amphetamine. Results suggest that amphetamine may act by more than one mechanism to inhibit eating. 21 references. (Author abstract modified)

**003104** Calvino, B.; Lagowska, J.; Ben-Ari, Y. Laboratoire de Physiologie nerveuse, Departement de Neurophysiologie appliquee, CNRS, F-91190 Gif-sur-yvette, France **Morphine withdrawal syndrome: differential participation of structures located within the amygdaloid complex and striatum of the rat.** Brain Research. 177(1):19-34, 1979.

The involvement of amygdaloid and striatal structures in the various signs of the morphine withdrawal syndrome was examined in male Wistar rats. The jump sign was elicited by local application of naloxone in the vicinity of the central nucleus of the amygdala or the lateral anterior nucleus, but not in adjacent amygdaloid or striatal nuclei. Diarrhea was more frequently elicited by application of naloxone in the striatum or centromedial amygdala than in the basolateral parts of the complex. No specific anatomical correlates to wet shakes, paw tremor, teeth chattering, and chewing were found. Bilateral electrolytic lesion of the central amygdala or combined transection of the stria terminalis and ventral amygdalofugal pathway eliminated the jump sign without affecting the remaining signs. A large bilateral lesion of the entire striatum did not significantly affect the various signs, and bilateral transection of the stria terminalis reduced only the occurrence of wet shakes. Transection of the medial forebrain bundle reduced jump, wet shakes, and diarrhea. 66 references. (Author abstract modified)

**003105** Canon, Jeffrey G. Dept. of Pharmacology, Schering Corporation, 60 Orange Street, Bloomfield, NJ 07003 **A comparison of clozapine, chlorpromazine, and thioridazine upon DRL performance in the squirrel monkey.** Psychopharmacology. 64(1):55-60, 1979.

Clozapine (0.16 to 10mg/kg orally), chlorpromazine (0.25 to 2mg/kg orally), and thioridazine (0.25 to 2mg/kg orally) were administered to squirrel monkeys subjected to a differential reinforcement of low rates (DRL) 10 sec schedule. The reinforcer consisted of 50% unsweetened orange juice. Chlorpromazine and thioridazine had no effect at the lower doses, but decreased response rate at the highest dose. Clozapine increased response rates at the low doses (0.31 to 2.5mg/kg) and decreased rates at the high dose (10mg/kg). Thus, clozapine appears to show a major difference from other neuroleptic drugs in this test by increasing response rate. Since clozapine produces few extrapyramidal side-effects in man, this procedure may be useful in selecting and developing new antipsychotic drugs with less liability for side-effects. 30 references. (Author abstract)

**003106** Cappell, Howard; Poulos, Constantine X. Addiction Research Foundation, 33 Russell Street, Toronto, Ontario M5S 2S1, Canada **Associative factors in drug pretreatment effects on gustatory conditioning: cross-drug effects.** Psychopharmacology. 64(2):209-213, 1979.

In an examination of the pretreatment effect (PE) in gustatory avoidance conditioning (e.g., reduction of a drug's ability to induce taste aversion by pretreatment with that drug), rats were pretreated with saline or amphetamine and exposed to a nonreinforcement procedure prior to testing for acquisition of an aversion to saccharin conditioned by amphetamine or morphine. The PE was obtained regardless of the drug used in conditioning. The associative manipulation involving nonreinforced presentation of the drug administration cues (injections followed by saline instead of drug) attenuated the PE when pretreatment and conditioning were with amphetamine, and was also effective when pretreatment was with amphetamine and conditioning was with morphine. Findings are interpreted within a framework of compensatory conditioning of a general physiological mechanism common to all gustatory avoidance. 14 references. (Author abstract modified)

**003107** Carroll, Marilyn E.; Meisch, Richard A. Psychiatry Research Unit, Mayo Box 392, University of Minnesota, Minneapolis, MN 55455 **The effects of feeding conditions on drug-reinforced behavior: maintenance at reduced body weight versus availability of food.** Psychopharmacology. 68(2):121-124, 1980.

The effects of food deprivation on drug self-administration were studied in male Wistar rats maintained at reduced body weights. Etonitazene hydrochloride was used as the reinforcer. Results showed that the reduced body weight, rather than the absence of food, was responsible for the increased rates of drug reinforced behavior seen in food deprived animals. 7 references. (Author abstract modified)

**003108** Castellano, Claudio. Laboratorio di Psicobiologia e Psicofarmacologia del C.N.R., Via Reno 1, I-00198 Rome, Italy **Effects of mescaline and amphetamine on simultaneous visual discrimination in two inbred strains of mice.** Psychopharmacology. 62(1):35-40, 1979.

The effects of mescaline and amphetamine were investigated in BALB/cJ (BALB) and C57BL/6J (C57) mice using the five choice Yerkes-Thompson Bryant-Bovet-Nitti apparatus for pattern discrimination. In experiment 1, pretrial administration of 5, 10, and 20mg/kg mescaline was followed by performance improvement in C57 Ss, while BALB Ss were impaired by the treatment as compared with saline controls. Pretrial administration of 0.1, 0.25, and 0.5mg/kg amphetamine improved performance in both strains. The same effects as in the pretrial experiment were noted in experiment 2 following administration of 20mg/kg mescaline and 0.5mg/kg amphetamine immediately after each session. No effect occurred 2 h after training, suggesting that pretrial effects were due to influences of the drugs on the consolidation processes of the two mouse strains. 36 references. (Author abstract modified)

**003109** Cazala, Pierre. Laboratoire de Psychophysiologie, University de Bordeaux 1, Institut de Biologie animale, Avenue des Facultes, 33405 Talence Cedex, France **Effects of clonidine and phentolamine on self-stimulation behavior in the dorsal and ventral regions of the lateral hypothalamus in mice.** Psychopharmacology. 68(2):173-177, 1980.

Intracranial self-stimulation (ICSS) of the dorsal and ventral regions of the lateral hypothalamus was studied in C57BL/6 mice treated with clonidine, which stimulates alpha-noradrenergic receptors, or phenotolamine, which blocks these receptors. Low doses (5mcg/kg i.p.) of clonidine depressed ventral hypothalamic ICSS but slightly increased dorsal ICSS; at higher doses of clonidine, ICSS was perturbed at both sites. Phentolamine depressed dorsal ICSS more than ventral ICSS. 32 references. (Author abstract modified)

**003110** Chance, William T.; Rosecrans, John A. Program in Pharmacology, N. E. Ohio Universities College of Medicine, Rootstown, OH 44272 **Lack of cross-tolerance between morphine and autoanalgesia.** Pharmacology Biochemistry and Behavior. 11(6):639-642, 1979.

The acquisition of autoanalgesia (behaviorally-induced antinociception) was investigated in morphine tolerant and nontolerant rats. Tolerance to morphine did not affect analgesia acutely elicited by a brief (15 second) schedule of footshock. Similarly, analgesia elicited by classically conditioned fear was not attenuated by morphine tolerance. These data suggest that endorphins may not be the principle mediators of autoanalgesic phenomena. 23 references. (Author abstract modified)

**003111** Chance, William T.; Rosecrans, John A. Program in Pharmacology, N. E. Ohio Universities College of Medicine, Rootstown, OH 44272 **Lack of effect of naloxone on autoanalge-**

**sia.** Pharmacology Biochemistry and Behavior. 11(6):643-646, 1979.

The effects of naloxone on autoanalgesia (behaviorally-induced antinociception) were investigated. Large doses of naloxone failed to modify antinociception elicited by acute footshock or conditioned fear in rats. Naloxone was also ineffective against antinociception following footshock in mice. These data suggest that if an endorphin does mediate autoanalgesia, the affinity of its receptor for naloxone is very low. Alternatively, parallel opioid and nonopioid systems may be activated by autoanalgesic procedures, with antagonisms of the opioid component being insufficient to reduce the antinociception. 24 references. (Author abstract modified)

**003112** Chapman, L. F.; Sassenrath, E. N.; Goo, G. P. Dept. of Behavioral Biology, School of Medicine, University of California, Davis, CA 95616 **Social behavior of rhesus monkeys chronically exposed to moderate amounts of delta9-tetrahydrocannabinol.** In: Nahas, G., Marihuana: biological effects. Oxford, Pergamon, 1979. 777 p. (p. 693-712).

The actions of delta9-tetrahydrocannabinol (THC) on the social behavior of rhesus and fascicularis macaque monkeys were studied following daily oral administration for periods of up to several years. Findings reveal that with the treatment schedule and dosage employed, sedative effects predominated for the first 2 to 3 months; a few animals intermittently exhibited a form of behavioral activation with increased pacing and other repetitive stereotyped behavioral patterns. With the treatment schedule held constant, tolerance to these behavioral effects was apparent thereafter. As these acute effects diminished, irritability and aggressiveness in treated animals increased significantly; this behavioral change was apparently not a withdrawal effect. At this stage previously lower ranked animals began to rise in the dominance hierarchy; overt aggression increased in treated animals and submissive behavior increased in nontreated cagemates. Findings suggest that repeated exposure to moderate amounts of THC over long periods results in a biologically serious impairement in ability to exhibit appropriately adaptive behavior. 78 references. (Author abstract modified)

**003113** Cheng, Richard S. S.; Pomeranz, Bruce. Zoology Dept., University of Toronto, Toronto, Ontario M5S 1A1, Canada **A combined treatment with d-amino acids and electroacupuncture produces a greater analgesia than either treatment alone; naloxone reverses these effects.** Pain. 8(2):231-236, 1980.

Naloxone reversible analgesia was produced in female B6AF1/J mice by electroacupuncture (EA) or by the D-amino acids (DAA) D-phenylalanine and D-leucine. EA combined with DAA had additive effects, which could also be blocked by naloxone. Only 62% of the animals showed marked analgesia when given combined EA and DAA treatment. 9 references. (Author abstract modified)

**003114** Chesher, G. B.; Zaluzny, S. G.; Jackson, D. M.; Malor, R. Dept. of Pharmacology, University of Sydney, New South Wales 2006, Australia **Delta9-tetrahydrocannabinol and the quasi morphine withdrawal syndrome.** In: Nahas, G., Marihuana: biological effects. Oxford, Pergamon, 1979. 777 p. (p. 605-618).

The effect of morphine in suppressing the quasi morphine withdrawal syndrome (QMWS) was compared with that of delta9 tetrahydrocannabinal(THc), haloperidol, and chlordiazepoxide, using male rats. Animals were observed for 20 QMWS signs. Data were analyzed by the number of animals exhibiting each sign, the mean withdrawal score, and the total number of signs exhibited. Results show that: 1) morphine significantly supressed th QMWS as expressed by the mean withdrawal score and the total number of signs exhibited; 2) THC significantly and dose dependently attenuated the QMWS when assessed as the mean withdrawal score: 3) only in the higher doses did haloperidol exert any significant effect on the mean withdrawal score, and was without effect at any dose level on the mean number of signs exhibited; and 4) at the dose levels tested, chlordiazepoxide produced no significant effect on either mean withdrawal score, nor on the mean number of signs exhibited. 23 references.

**003115** Christie, Macdonald J.; Overstreet, David H. Overstreet: School of Biological Sciences Flinders University of South Australia, Bedford Park, 5042 South Australia **Sensitivity of morphine-tolerant rats to muscarinic and dopaminergic agonists: relation to tolerance or withdrawal.** Psychopharmacology. 65(1):27-34, 1979.

The relationship between subsensitivity and supersensitivity to dopamine and acetylcholine agonists and the states of morphine tolerance or withdrawal was investigated. Male hooded Wistar rats were treated chronically once daily with morphine sulphate after completing a session in an operant chamber. Periodic challenges with morphine prior to the operant session established that tolerance development was virtually complete within 10 days. The morphine treated rats were more sensitive to the behavioral suppressing effects of apomorphine, a dopamine agonist, and pilocarpine, an acetylcholine agonist, when administered in the tolerant state. Conversely, the morphine treated rats were less sensitive to both agonists when administered in the withdrawal state. The behavioral and neurochemical studies are consistent with the view that morphine tolerant rats are supersensitive to dopamine and acetylcholine agonists, and morphine withdrawn rats are subsensitive. 41 references. (Author abstract modified)

**003116** Clincke, G.; Wauquier, A. Dept. of Pharmacology, Janssen Pharmaceutica Research Laboratories, B-2340 Beerse, Belgium **Metrazol-produced impairment of passive-avoidance retention specifically antagonized by anti-petit mal drugs.** Psychopharmacology. 66(3):243-246, 1979.

When rats trained in stepdown avoidance were treated 30 minutes before a session with saline or a subconvulsive dose of metrazol, metrazol rats significantly failed to retain the avoidance task. Groups of six rats per dose were trained and 24 hours later pretreatment 5 minutes before metrazol, with an i.p. injection of the following antiepileptics: ethosuximide, trimenthadione, clonazepam, sodium valproate, carbamazepine, phenobarbital, diphenylhydantion, or high dose of haloperidol and amphetamine. Only ethosuximide, trimethadione, and clonazepam significantly increased the latency to stepdown and significantly shortened the time on the grid. Sodium valproate only shortened the time spent on the grid. Results suggest that only anti-petit mal drugs antagonize the retention impairment of passive-avoidance produced by metrazol. 11 reference. (Author abstract modified)

**003117** Cole, Sherwood O. Dept. of Psychology, Rutgers University, Camden, NJ 08102 **Deprivation-dependent effects of amphetamine on concurrent measures of feeding and activity.** Pharmacology Biochemistry and Behavior. 12(5):723-727, 1980.

The effects of d-amphetamine (0.5, 1.0, or 2.0mg/kg) on feeding, ambulatory activity, and rearing of male Holtzman rats were studied in an open-field arena after various periods of food deprivation (0, 24, 48, or 72 hours). Differences in the amount of food deprivation significantly altered the drug's effect on feeding and rearing, but not on ambulatory activity. The degree of food deprivation had a greater influence on the correlation between feeding and ambulatory activity than on the correlation

between rearing and feeding or ambulatory activity. 12 references. (Author abstract modified)

**003118** Collins, Catherine; Laird, R. I.; Richards, P. T.; Starmer, G. A.; Weyrauch, Solveig. Dept. of Pharmacology, University of Sydney, Sydney, NSW 2006, Australia **Aspirin-caffeine interaction in the rat.** Journal of Pharmacy and Pharmacology. 31(9):611-614, 1979.

High doses of aspirin (400mg/kg) or caffeine (5mg/kg) induced hyperactivity in female DA rats, but low doses of aspirin had no effect. Caffeine-induced hyperactivity lasted for about 2 hours, but aspirin-induced hyperactivity lasted from 1 to 6 hours after dosing. Simultaneous administration of the two drugs produced long lasting hyperactivity, even with doses of aspirin that showed no stimulant effects when given alone. Absorptive and metabolic effects did not appear to play a major role in the interaction. It is suggested that the sustained hyperactivity seen after combined drug administration may be due to enhanced effects of solicylate on central catecholamine utilization in the presence of a phosphodiesterase inhibitor. 12 references. (Author abstract modified)

**003119** Collins, Catherine; Laird, R.; Richards, P. T.; Starmer, G. A.; Weyrauch, Solveig. Dept. of Pharmacology, University of Sydney, NSW 2006, Australia **Aspirin-phenacetin interaction in the rat.** Journal of Pharmacy and Pharmacology. 31(9):632-633, 1979.

Plasma drug levels and locomotor activity were examined in female DA rats following separate and combined administration of aspirin and phenacetin. A progressive reduction in plasma phenacetin concentration was observed when increasing doses of aspirin were given with a constant dose of phenacetin; phenacetin also reduced plasma salicylate concentrations. Phenacetin (50 and 100mg/kg) had no effect on locomotor activity. Low doses of aspirin also failed to alter locomotor stimulation, but a 400mg/kg dose produced long lasting stimulation. Phenacetin enhanced this effect, even with a 200mg/kg dose of aspirin. It is suggested that salicylate effects on catecholamine utilization may be augmented in the presence of phenacetin (as they are in the presence of caffeine) as a result of phosphodiesterase inhibitor activity. 10 references.

**003120** Collins, Jeremiah P.; Lesse, Henry; Dagan, Lori A. Dept. of Psychiatry and Biobehavioral Sciences, School of Medicine, University of California, Los Angeles, CA 90024 **Behavioral antecedents of cocaine-induced stereotypy.** Pharmacology Biochemistry and Behavior. 11(6):683-687, 1979.

The effect of cocaine on discriminative behavior in cats was investigated in a study of behavioral antecedents of cocaine-induced stereotypy. Cats were trained in a discrimination task where bar-pressing when a tone was present (S) resulted in milk reinforcement. When the tone was absent (S-), milk was not delivered. The duration of these periods varied randomly during 30 minute sessions and responses during S- delayed the next trial. Once a high level of discrimination was achieved, drug testing was begun. Ongoing behavior was manipulated by scheduling either a 5 minute S or S- period immediately after cocain injection (1mg/kg). When S followed cocaine, stereotyped bar-pressing developed with markedly increased responding during the remainder of the session. In contrast, when S- followed cocaine, suppression of bar-pressing developed. The effect could be reversed in most Ss when stimulus conditions were later reversed. A similar experiment using rats yielded similar results. These results indicate that ongoing behavior and stimulus conditions are critically important in determining the behavioral effects of cocaine. 19 references. (Author abstract modified)

**003121** Cookson, Susan L.; Mann, J. Douglas. Mann: Dept. of Neurology, University of North Carolina, Chapel Hill, NC 27514 **Phenytoin reversal and prevention of morphine-induced catalepsy in the rat.** Pharmacology Biochemistry and Behavior. 12(5):743-746, 1980.

Phenytoin (35mg/kg i.v.) prevented or reversed catalepsy induced in male Sprague-Dawley rats by morphine (1mg/kg i.v.). Naloxone (0.2mg/kg) aiso antagonized the cataleptic effects of morphine. Results support the hypothesis that catalepsy depends specifically on changes in synaptosomal calcium metabolism. 17 references. (Author abstract modified)

**003122** Cooper, Steven J.; Francis, Raymond L. Dept. of Psychology, University of Birmingham, P.O. Box 363, Birmingham BI5 2TT, England **Food-choice in a food-preference test: comparison of two mouse strains and the effects of chlordiazepoxide treatment.** Psychopharmacology. 65(1):89-93, 1979.

The effects of chlordiazepoxide (CDP) treatment on the feeding behavior of mice in the food preference test used previously with rats (Cooper and Crummy, 1978) were examined. In C57 male mice, CDP reduced the latency to begin eating and prolonged the total time devoted to eating. In contrast, in A2G male mice, CDP did not reduce the latency to begin eating and only prolonged the total time devoted to eating at a single dose level, 5.0 mg/kg. The two strains differed in their choice between novel and familiar foods that were concurrently available in the test. CDP at all doses increased the duration of eating devoted to familiar food in the C57 animals, but did not increase feeding duration in the A2G mice. However, CDP increased the time spent eating novel foods in both strains to the same degree. Possible mechanisms underlying the effect of CDP on food preference behavior in mice and accounting for the strain difference in response to CDP are considered. 10 references. (Author abstract modified)

**003123** Cooper, Steven J.; Posadas-Andrews, Astrid. Dept. of Psychology, University of Birmingham, P.O. Box 363, Birmingham BI5 2TT, England **Food and water intake in the non-deprived pigeon after chlordiazepoxide administration.** Psychopharmacology. 65(1):99-101, 1979.

A selective increase in feeding brought about by chlordiazepoxide in the pigeon is demonstrated. Food and water intake were measured in nondeprived pigeons over a 4 h period during daytime. Under control conditions, the ratio of food to water intake was approximately 1:1, and both intakes were a simple linear function of time. Chlordiazepoxide doubled the mean amount of food intake, while leaving water intake unchanged. This is a first indication that chlordiazepoxide can selectively stimulate appetite for food in an avian species. Some birds showed sedation following a first acute injection; its duration was shortened after repeated injections, and the hyperphagic response to the drug was revealed. 14 references. (Author abstract modified)

**003124** Costall, Brenda; Fortune, David H.; Hui, Siu-Chun G.; Naylor, Robert J. Postgraduate School of Studies in Pharmacology, University of Bradford, Bradford BD7 1DP, England **Neuroleptic antagonism of the motor inhibitory effects of apomorphine within the nucleus accumbens: drug interaction at presynaptic receptors?** European Journal of Pharmacology. 63(4):347-358, 1980.

Injection of d-amphetamine into the nucleus accumbens of male Sprague-Dawley rats caused a dose dependent hyperactivity due to release of newly synthesized dopamine. This hyperactivity was antagonized by injection of apomorphine into the nucleus accumbens. Results suggested that apomorphine was acting at neuroleptic sensitive, presynaptic sites within the nu-

cleus accumbens. Additional data suggested that more than one neuroleptic mechanism in the nucleus accumbens may contribute to the overall control of motor function via the mesolimbic system. 33 references. (Author abstract modified)

**003125** Costall, Brenda; Hui, Siu-Chun G.; Naylor, Robert J. Postgraduate School of Studies in Pharmacology, University of Bradford, Bradford, West Yorkshire, England **Differential effects of (3,4-dihydroxyphenylamino)-2-imidazoline (DPI) on hyperactivity responses to dopamine agonists injected into the nucleus accumbens.** Journal of Pharmacy and Pharmacology. 31(7):478-480, 1979.

The influence of (3,4-dihydroxyphenylamino)-2-imidazoline (DPI) on the hyperactivity induced in rats by intraaccumbens injection of dopamine, d-amphetamine, ergometrine, or 2-(N,N-diethyl)amino-5,6-dihydroxy-1,2,3,4-tetrahydronaphthalene (ATN compound) was examined. The hyperactivity responses caused by 6.5mcg amphetamine or 1mcg ergometrine were reduced or abolished by subsequent injection of 5 to 10mcg DPI into the nucleus accumbens, but hyperactivity induced by 50mcg dopamine (after pretreatment with 100mg/kg i.p. nialamide) or by 1.56 to 12.5mcg of the ATN compound was resistant to DPI. These findings are discussed in relation to the hypothesis that two functionally distinct dopamine receptor mechanisms in the nucleus accumbens are involved in locomotor hyperactivity. 10 references.

**003126** Cunningham, Christopher L.; Linakis, James G. University of Oregon Health Sciences Center, Portland, OR 97201 **Paradoxical aversive conditioning with ethanol.** Pharmacology Biochemistry and Behavior. 12(3):337-341, 1980.

In three experiments with hooded rats, paired injections of ethanol and lithium chloride produced an aversion to the taste of ethanol, yet reduced ethanol's potency as an unconditioned stimulus during subsequent taste aversion conditioning with saccharin (paradoxical aversive conditioning). Two of the experiments were designed to test an associative blocking account of the latter findings. In each of these experiments, an attempt was made to extinguish the aversion conditioned to a potential blocking stimulus after ethanol/lithium pairings, but before saccharin/ethanol conditioning. Nonreinforced exposure to i.p. mediated ethanol taste cues did not eliminate the detrimental effect of ethanol/lithium pairings on subsequent saccharin/ethanol conditioning, whereas nonreinforced exposure to handling injection cues did, thus providing support for the associative blocking interpretation. Implications of these findings for chemical aversion therapy are discussed. 11 references. (Author abstract modified)

**003127** Curley, M. D.; Walsh, J. M.; Burch, L. S. Behavioral Sciences Dept., Naval Medical Research Institute, Bethesda, MD 20014 **Behavioral effects of morphine on free-operant avoidance under hyperbaric pressure.** Pharmacology Biochemistry and Behavior. 12(3):413-417, 1980.

The behavioral effects of morphine on free operant avoidance were assessed under hyperbaric pressure. Four male hooded rats were trained to avoid brief electric shocks under a free operant unsignalled avoidance procedure. Using an individual organism design, rats were tested at 1.0 and 7.1 atmospheres absolute (ATA) in a dry hyperbaric chamber while breathing a mixture of helium and oxygen. Rats were injected s.c. with morphine sulfate (2.0, 4.0, 6.0, 8.0mg/kg) or saline and observed during the 1 hour session. Overall, the analgesic effects of morphine at 1.0 and 7.1 ATA were found to be similar. Shock avoidance by the Ss was found to be a monotonic function of drug dose. Increased pressure did not significantly affect the number of shocks received by a rat across doses. Total responding remained stable throughout the study, but the temporal pattern of responding was differentially influenced by drug dose. 18 references. (Author abstract modified)

**003128** Curzon, G.; Fernando, J. C. R.; Lees, A. J. Dept. of Neurochemistry, Institute of Neurology, 33 John's Mews, London WC1N 2NS **Backward walking and circling: behavioural responses induced by drug treatments which cause simultaneous release of catecholamines and 5-hydroxytryptamine.** British Journal of Pharmacology. 66(4):573-579, 1979.

Backward walking and circling were studied in male Sprague-Dawley rats given i.p. injections of 15mg/kg d-amphetamine, p-chloroamphetamine, or fenfluramine or 5mg/kg fenfluramine. Characteristic dopamine dependent behaviors such as rearing, licking, and gnawing resulting from d-amphetamine were greatly reduced by p-chloramphetamine or fenfluramine. The serotonin dependent behaviors (wet dog shake and hind limb abduction) caused by fenfluramine or p-chloroamphetamine were not affected by d-amphetamine. Fragmentary backward walking and circling resulting from injection of 50mg/kg levallorphan were decreased by low doses of d-amphetamine. These findings support the view that backward walking and circling are mediated by simultaneous dopamine and 5-HT release. Results are discussed in relation to hallucinogenic activity, amphetamine psychosis, schizophrenia, and drug-induced tardive dyskinesia. 33 references. (Author abstract modified)

**003129** Dahlof, Lars-Gosta; Larsson, Knut. Dept. of Psychology, Unit of Psychobiology, University of Goteborg S-400 20 Gothenburg, Sweden **PCPA potentiates the effects of specific copulatory experience on the sexual behavior of the pudendectomized male rat.** Pharmacology Biochemistry and Behavior. 11(6):701-704, 1979.

The interactional effects of bilateral pudendectomy and sexual experience on the sexual behavior of male rats were studied, and the influence of para-chlorophenylalanine (PCPA) on these effects was examined. In Experiment 1, limited sexual experience in terms of mounts, intromissions, or ejaculations was provided prior to the operation. The sexual behavior was then tested before and after treatment with PCPA, a drug known to increase the sexual activity of male rats. In Experiment 2, massive sexual experiences were provided the animals prior to pudendectomy, and sexual behavior was tested with or without PCPA treatment. No variety of limited sexual experience differentiated the effects of pudendectomy. After PCPA treatment, however, the intromittive and ejaculatory capacity of all experienced animals improved significantly. In animals with massive sexual experience, the behavioral dysfunctions sfter pudendectomy were even more dramatically counteracted by PCPA treatment. 11 references. (Author abstract modified)

**003130** DaVanzo, John P.; Sydow, M. East Carolina University, School of Medicine, Greenville, NC 27834 **Inhibition of isolation-induced aggressive behavior with GABA transaminase inhibitors.** Psychopharmacology. 62(1):23-27, 1979.

The effects of aminooxyacetic acid (AOAA) administrations and gamma-acetylenic GABA (GAG) administrations on the aggressive behavior of isolated male albino mice were investigated. Both compounds resulted in a dose dependent suppression of aggressiveness and a concomitant increase in brain GABA. The increase in GABA levels persisted beyond the time when AOAA and GAG exerted an anti aggressive effect. Brain GABA levels remained significantly elevated over controls for 120 h after a single injection of AOAA and 46 h after a single dose of GAG. 28 references. (Author abstract)

**003131** Davis, Kenneth L.; Hollister, Leo E.; Vento, Adela L.; Beilstein, Barbara A.; Rosekind, Gary R. Psychiatric Clinical

Research Center, Stanford University, 3801 Miranda Avenue, Palo Alto, CA 94304 **Dimethylaminoethanol (Deanol): effect on apomorphine-induced stereotypy and an animal model of tardive dyskinesia.** Psychopharmacology. 63(2):143-146, 1979.

The effects of dimethylaminoethanol (DMAE) on apomorphine-induced stereotypy was investigated in rats. A dose of 80mg of DMAE had no effect on the severity of apomorphine-induced stereotypy. However, 160mg of DMAE significantly diminished the severity of apomorphine-induced stereotypy. This dose of DMAE did not significantly alter spontaneous locomotor activity. DMAE did not reduce apomorphine-induced stereotypy in animals previously exposed to haloperidol and presumed to have post-synaptic dopamine receptor supersensitivity. These results with DMAE are contrasted with the effects of choline chloride, and suggest that choline chloride may be more effective than DMAE at augmenting striatal cholinergic activity. 28 references. (Author abstract)

**003132** Davis, Michael. Yale University, School of Medicine, 34 Park Street, New Haven, CT 06508 **Diazepam and flurazepam: effects on conditioned fear as measured with the potentiated startle paradigm.** Psychopharmacology. 62(1):1-7, 1979.

The effects of two antianxiety drugs in the benzodiazepine class (diazepam or Valium and flurazepam or Dalmane) on the potentiated startle response of rats were investigated. Doses of 0.3, 0.6, 1.2, or 2.5mg/kg of diazepam produced a dose dependent reduction of the potentiated startle effect where acoustic startle amplitude is normally increased in the presence of a light previously paired with a shock. The primary effect of diazepam was to block expression of, rather than acquisition of, fear as measured by the potentiated startle. Doses of 2.5, 10, or 20mg/kg of flurazepam also reduced the startle selectively but was 6 to 8 times less potent than diazepam. These results suggest that the potentiated startle paradigm, as a measure of classical conditioning that involves no operant, might be a useful adjunct to behavioral methods currently used in analyzing antianxiety compounds. 17 references. (Author abstract modified)

**003133** Davis, W. Marvin; Werner, Toreen E.; Smith, Stanley G. Dept. of Pharmacology, School of Pharmacy, University of Mississippi, University, MS 38677 **Reinforcement with intragastric infusions of ethanol: blocking effect of FLA 57.** Pharmacology Biochemistry and Behavior. 11(5):545-548, 1979.

The ability of FLA 57, a dopamine beta-hydroxylase inhibitor, to block the reinforcing action of ethanol in rates was tested under two circumstances, when the drug was self-administered by intragastric (IG) infusion and when it was used to establish a conditioned reinforcer. FLA 57 had previously been reported to suppress oral intake of ethanol by rats. The results demonstrated the ability of FLA 57 to suppress bar-pressing for intragastric delivery of doses of ethanol. This indicates that the effect on oral intake of ethanol may not be attributed to a taste factor. The same dose of FLA 57 did not suppress responding for IG doses of sweet milk. Thus, there was not an impairment of appetitive behavior in general through some nonspecific depressant or toxic action. Furthermore, the primary reinforcing action of ethanol, when used to establish a buzzer as a conditioned reinforcer through repeated pairings, was blocked if FLA 57 was given before pairings. This was evidenced by a failure of such rates to bar-press above the baseline level in a later test of conditioned reinforcement, which contrasted with the increased responding seen for rates receiving saline instead of FLA 57 before ethanol. These data support the previous findings of oral ethanol and confirm that FLA 57 can impair the mechanism by which ethanol produces positive reinforcement in rats. 15 references. (Author abstract modified)

**003134** de Angelis, Luisa; File, Sandra E. Universita degli Studi di Trieste, Istituto di Farmocologia, Via A. Valerio N. 32, Trieste, Italy **Acute and chronic effects of three benzodiazepines in the social interaction anxiety test in mice.** Psychopharmacology. 64(2):127-129, 1979.

The effects on social interaction of acute and chronic dosage with diazepam (1mg/kg), desmethyldiazepam (2mg/kg), and chlordesmethyldiazepam (.125mg/kg) were studied in pairs of mice. The mice were tested under either high or low levels of illumination. In all cases, acute drug treatment significantly reduced social interaction, but this was not seen with chronic (9 days) treatment. Two of the drugs, diazepam and desmethyldiazepam, showed an anixiolytic action, i.e., these drugs resulted in significantly less variation in social interaction with change in light levels, compared with vehicle injected controls. 17 references. (Author abstract)

**003135** de Caro, Giuseppe; Massi, Maurizio; Micossi, Luigi G. Institute of Pharmacology and Pharmacognosy, University of Camerino, I-62032 Camerino, Italy **Modifications of drinking behaviour and of arterial blood pressure induced by tachykinins in rats and pigeons.** Psychopharmacology. 68(3):243-247, 1980.

Intracerebroventricular injections of the naturally occurring tachykinins eledoisin, physalaemin, and substance-P had a powerful antidipsogenic effect in male Wistar rats, but markedly stimulated water intake in pigeons. The three peptides induced a fall in arterial blood pressure in both species. These findings suggest that the effect of these peptides on water intake is not related to their vascular effects and may be specific to the CNS. 17 references. (Author abstract modified)

**003136** de Wied, D.; van Ree, J. M.; Greven, H. M. Rudolf Magnus Institute for Pharmacology, Medical Faculty, University of Utrecht, Vondellaan 6, Utrecht, The Netherlands **Neuroleptic-like activity of peptides related to (DES-TYR1) gamma-endorphin: structure activity studies.** Life Sciences. 26(19):1575-1579, 1980.

The potency of various fragments of gamma-endorphin (beta-LPH61-77) was compared on their ability to facilitate extinction of pole jumping avoidance behavior and their effects in two grip tests used as measures of neuroleptic-like activity. It appears that beta-LPH66-71 is the shortest sequence which shows potencies in the three tests comparable to that of DTgammaE (beta-LPH62-77). The activity of beta-LPH67-77 was less. It is proposed that LPH66-77 rather than DTgammaE represents an endogenous neuroleptic-like neuropeptide which may play a key role in psychopathology. 8 references. (Author abstract)

**003137** Delay, Eugene R.; Isaac, Walter. Isaac: Dept. of Psychology, University of Georgia, Athens, GA 30602 **The effects of illumination, d-amphetamine, and methylphenidate upon vigilance performance of squirrel monkeys.** Bulletin of the Psychonomic Society. 15(4):203-206, 1980.

The effects of illumination, d-amphetamine, and methylphenidate on vigilance behavior were studied with four squirrel monkeys. Detection rates of an auditory signal were higher in the light than in the dark. Although methylphenidate did not alter performance, d-amphetamine lowered detection rates more in the light than in the dark, particularly in male squirrel monkeys. It is concluded that the results may be interpreted in terms of altered arousal levels. 35 references. (Author abstract modified)

**003138** Della-Fera, Mary Anne; Baile, Clifton A. Dept. of Clinical Studies, School of Veterinary Medicine, University of Pennsylvania, New Bolton Center, Kennett Square, PA 19348 **Cerebral ventricular injections of CCK-octapeptide and feed**

**intake: the importance of continuous injection.** Physiology & Behavior. 24(6):1133-1138, 1980.

A 30.6pmole intracerebroventricular dose of cholecystokinin octapeptide (CCK-OP) reduced feed intake in sheep by 80% when given a continuous injection over 45 minutes, but had no effect on feed intake when given as one, four, or eight bolus injections. Feed intakes were significantly lower when the CCK-OP continuous injections was begun 15 minutes before the meal than when the injection began immediately before or 5 minutes before the meal. This finding suggests that CCK-OP may act outside the immediate vicinity of the lateral ventricles to suppress feeding. 23 references. (Author abstract modified)

**003139** Dhume, V. G.; Pereira, J. S.; Diniz, R. S.; Abraham, G. J. S. Dept. of Pharmacology, Goa Medical College, Panjim, Goa, India **Contraction of cat nictitating membrane by tetramisole.** Archives Internationales de Pharmacodynamie et de Therapie. 238(1):14-18, 1979.

The antidepressant tetramisole produced a dose dependent, persistent contraction of cat nictitating membrane. This effect was abolished by pretreatment with phenoxybenzamine, but not by pretreatment with reserpine or tyramine or by adrenalectomy. These findings suggest that tetramisole has a direct stimulant action on alpha-adrenergic receptors of cat nictitating membrane. No contraction of the nictitating membrane was observed following treatment with imipramine, indicating that the effect is not common to all antidepressants. 6 references. (Author abstract modified)

**003140** Dobrzanski, S.; Doggett, N. S. Dept. of Pharmacy, Bradford Royal Infirmary, Bradford, England **The effect of propranolol phentolamine and pimozide on drug-induced anorexia in the mouse.** Psychopharmacology. 66(3):297-300, 1979.

The role of catecholamines (CA) in the anoretic action of amphetamine, as well as diethylpropion, mazindol, and phentermine,, three antiobesity agents in current clinical use, was examined in the mouse, Pimozide was a potent antagonist of amphetamine, diethylpropion, mazindol, and phentermine anorexia in the mouse. Phentolamine and propranolol produced no such antagonism, but either potentiated or had no effect on the drug-induced anorexia. Although the mechanism of action of the four anorectic agents appears to involve dopamine receptor agonist activity, it is suggested that an antagonist or partial agonist effect at noradrenergic receptors may also be involved. 11 references. (Author abstract modified)

**003141** Dodd, P. R.; Bradford, H. F.; Abdul-Ghani, A. S.; Cox, D. W. G.; Continho-Netto, J. Bradford: Dept. of Biochemistry, Imperial College, London SW7 2AZ, England **Release of amino acids from chronic epileptic and subepileptic foci in vivo.** Brain Research. 193(2):505-517, 1980.

Perforated discs of cobalt (Co) or nickel (Ni) were implanted onto the sensorimotor strip of the cerebral cortex in female hooded Rowett rats. Co discs induced myoclonic contralateral limb jerks, but overt limb jerks were not observed in Ni implanted rats. Superfusion of Co or Ni with an in vivo cannula system resulted in increased release of glutamate, valine, and glycine compared to unlesioned tissue. Release from epileptogenic Co lesions was about three times greater than that from nonepileptogenic lesions. The epileptogenic lesions also caused a marked reduction in glutamine release. 54 references. (Author abstract modified)

**003142** Domjan, Michael; Gemberling, Gail A.; Gillan, Douglas J. Dept. of Psychology, University of Texas, Austin, TX 78712 **Increased drinking stimulated by exposure to lithium-conditioned taste cues: effects of conditioning trials and drug dose.** Pharmacology Biochemistry and Behavior. 12(5):789-795, 1980.

Sprague-Dawley rats exposed to a lithium conditioned taste solution subsequently drank more of a palatable vanilla solution than did rats exposed to tap water or a taste solution not paired with lithium. This enhanced drinking effect was observed with a large range of procedures. However, the enhanced drinking was not closely related to the degree of aversion animals acquired to the lithium paired solution. 10 references. (Author abstract modified)

**003143** Donoso, A. O.; Broitman, S. T. Consejo Nacional de Investigaciones Cientificas y Tecnicas de Argentina (CONICET), Buenos Aires, Argentina **Effects of a histamine synthesis inhibitor and antihistamines on the sexual behavior of female rats.** Psychopharmacology. 66(3):251-255, 1979.

The effects of drugs which in different ways alter endogenous histamine activity were studied and the lordotic responses of ovariectomized estradiol plus progesterone primed femal rats injected in the lateral ventricle with the drugs was evaluated . Alpha-hydrazinohistidine produced a significant decrease of lordotic responses and sexual receptivity. The H1-antihistamines pyrilamine and chlorfeniramine and the H2-antihistamine metiamide significantly decreased the lordosis quotient but did not modify receptivity. Antishistamine injected rats showed no soliciting behavior. Exploratory activity was decreased by alpha-hydrazinohistidine and metiamide but not by the H1-antihistamines. It is concluded that treatments which either deplete histamine or block their receptors can alter female copulatory responsiveness. The mechanism of this antihistamine effect is suggested to be unrelated to that of other side-effects, such as motor impairment, sedation, or local anesthesia. 26 references. (Author abstract modified)

**003144** Dooley, David James. University of Washington **A pharmacological analysis of d-amphetamine-induced inhibition of food-reinforced operant behavior in Macaca fascicularis. (Ph.D. dissertation).** Dissertation Abstracts International. 40(12):5616-B, 1980. Ann Arbor, Univ. Microfilms No. 8013518, 129p., 1979.

The pharmacological mechanisms underlying the d-amphetamine-induced inhibition of food reinforced operant behavior were investigated in Macaca fascicularis using a chain schedule designed to be selectively sensitive to response inhibition and response excitation produced by indirect and direct acting catecholaminergic agonists. The primary effect of d-amphetamine on operant behavior was response inhibition. Injections of other catecholaminergic agonists demonstrated that the response inhibition is: 1) a central phenomenon lacking a peripheral contribution, 2) a function of the indirect release of dopamine, 3) the possible result of an interaction between different subpopulations of dopaminergic receptors, and 4) minimally dependent on alpha and beta receptors. Response inhibition was also shown to be not directly attributable to anorexia. The effects of catecholaminergic agonists on operant behavior are discussed with reference to mechanisms of action on catecholaminergic systems and on subpopulations of catecholaminergic receptors. (Journal abstract modified)

**003145** Dray, Susan Marguerite. University of California, Los Angeles **Behavioral and physiological sequelae of ACTH and ACTH4-10 administration during infancy in rats. (Ph.D. dissertation).** Dissertation Abstracts International. 41(1):398-B, 1980. Ann Arbor, Univ. Microfilms No. 8016071, 183p., 1980.

Behavioral and physiologcal sequelae of adrenocorticotropic hormone (ACTH) and ACTH4-10 administration during infancy were investigated in rats. Two hundred twenty-one infant rats were treated with ACTH4-10 on days 7 through 9, and a condi-

tioned taste aversion (CTA) was induced on day 12 by pairing a taste (apple juice) with LiCl-induced illness. Pups were tested for evidence of acquisition on day 15, for evidence of retention on day 22, or both. Results of this and other experiments indicate that young animals are influenced by ACTH1-39 given on days 7 through 9. The exact effects of ACTH4-10 over these same days remains enigmatic. However, there are acute effects of this analogue on retrieval of learning of a salutory nature, which suggests that the young animal is capable of a presumably more adult type of learning than previously supposed as well as being able to respond behaviorally to this peptide. (Journal abstract modified)

**003146** Drew, G. M.; Gower, Alma J.; Marriott, A. S. Dept. of Pharmacology, Glaxo-Allenburys Research Ltd., Ware, Hertfordshire SG12 0DJ, England **Alpha2-adrenoceptors mediate clonidine-induced sedation in the rat.** British Journal of Pharmacology. 67(1):133-141, 1979.

The sensitivity toward alpha-adrenoceptor agonists and antagonists of the central alpha-receptors that mediate clonidine-induced sedation was examined in AH/H male hooded rats. Intracerebroventricular (i.c.v.) and i.p. injections of clonidine caused dose dependent sedation. Similar effects were obtained with i.c.v. administration of xylazine, naphozoline, and methoxamine, but not phenylephrine. The sedation induced by i.p. clonidine was antagonized by i.c.v. phentolamine, yohimbine, piperoxan, and tolazine, but not by labetalol, thymoxamine, or prazosin. The relative potencies of the agonists in causing sedation and of the antagonists in inhibiting the sedative effect of clonidine indicated that the central alpha-receptors involved in clonidine sedation are similar to peripheral presynaptic alpha2-adrenoceptors. 38 references. (Author abstract modified)

**003147** Dudek, Bruce C.; Fanelli, Richard J. Dept. of Psychology, SUNY, 1400 Washington Ave., Albany, NY 12222 **Effects of gamma-butyrolactonee, amphetamine, and haloperidol in mice differing in sensitivity to alcohol.** Psychopharmacology. 68(1):89-97, 1980.

The duration of the loss of righting reflex induced by gamma-butyrolactone (GBL) was greater in mice selectively bred for greater sensitivity to ethanol (LS) than in less sensitive SS mice. GBL also induced a threefold greater increase in brain dopamine levels in LS mice than in SS mice. The inbred strains BALB/c, DNA/2, and C57BL/6 showed decreasing order of response to GBL. GBL had biphasic effects of locomotor activity, and the initial depression and subsequent increase in activity were both greater in LS than in SS mice. 36 references. (Author abstract modified)

**003148** Duncan, Perry M.; Phillips, Jerry; Reints, Jane; Schechter, Martin D. Schechter: Northeastern Ohio Universities College of Medicine, Rootstown, OH 44272 **Interaction between discrimination of drug states and external stimuli.** Psychopharmacology. 61(1):105-106, 1979.

Rats learned a two choice operant response by discriminating differences between external stimuli, internal (drug produced) stimuli, or a combination of these two types of stimuli in a discrimination study. A tactile and visual external cue was superior to the ethanol/saline cue in producing stimulus control, but the group receiving both drug and external stimulus cues performed in a manner very similar to the external cue only group. The two stimulus sources did not promote more rapid or complete discrimination. After acquisition of discrimination, previously coincident drug and external stimulus states were reversed to determine which stimulus source had more behavioral control. This test for stimulus selectivity indicated that the external stimulus had essentially complete control of response choice. 4 references. (Author abstract modified)

**003149** Dykstra, Linda A. Dept. of Psychology, University of North Carolina, Chapel Hill, NC 27514 **Meperidine's effects under shock titration and shock discrimination procedures.** Pharmacology Biochemistry and Behavior. 12(3):403-407, 1980.

Meperidine's effects were examined under a schedule of shock titration and under a shock intensity discrimination in which squirrel monkeys discriminated between the presence and absence of a low intensity shock. Meperidine did not increase the intensity at which monkeys maintained the shock in the shock titration procedure, nor did meperidine alter the percentage of correct responses under the shock intensity discrimination although meperidine did increase the time to respond in the presence and absence of shock. When meperidine was combined with a dose of SKF-525A which did not alter responding when given alone, the intensity at which monkeys maintained the shock under the shock titration procedure was increased. Moreover, the percentage of correct responses in the presence of shock under the shock titration procedure was decreased by the combination of meperidine and SKF-525A. 24 references. (Author abstract)

**003150** Dysken, Maurice W.; Steinberg, Joel; Davis, John M. Dept. of Psychiatry, University of Chicago, Pritzker School of Medicine, Chicago, IL 60615 **Sodium amobarbital response during simulated catatonia.** Biological Psychiatry. 14(6):995-1000, 1979.

Sodium amobarbital response during simulated catatonia was assessed in relation to the issue of volitional control in catatonia. Nine normal volunteers, and one recovered catatonic schizophrenic S were instructed in the simulation of catatonia, and tested at the simulation of catatonia following administration of sodium amobarbital. All Ss were able to simulate catatonic behaviors, suggesting that stuporous catatonia does not fit a model of volitionally controlled behavior. 11 references.

**003151** Dzoljic, M. R.; v. d. Lely, A. J.; v. Mourik, J. B. A. Dept. of Pharmacology, Medical School, Erasmus University, P. O. Box 1738, Rotterdam, The Netherlands **Enkephalin-induced myolonic twitches blocked by ergometrine and potentiated by haloperidol.** Psychopharmacology. 66(2):111-116, 1979.

Myoclonic twitches (MT) in the submandibular muscles induced by intraventricular administration of D-ala2-met-enkephalinamide (DALA) were studied electromyographically in the rat. Measurement of MT activity was selected since it permits parallel study of the effect of enkephalin on both dopaminergic and serotonergic transmitter systems. The twitches induced by enkephalin were blocked by naloxone, gamma-hydroxybutyrate, and ergometrine, but potentiated by haloperidol. Methysergide did not alter the stimulatory effect of DALA. These results are interpreted as a possibility for a specific enkephalin-induced activation of the so called inhibition mediating dopaminergic system, which is sensitive ti the blocking action of ergometrine, but resistant to the blocking action of haloperidol. 28 references. (Author abstract)

**003152** Ebstein, Richard P.; Eliashar, Shlomo; Belmaker, Robert H.; Ben-Uriah, Yehuda; Yehuda, Shlomo. Jerusalem Mental Health Center, Ezrath Nashim, POB 140, Jerusalem, Israel **Chronic lithium treatment and dopamine-mediated behavior.** Biological Psychiatry. 15(3):459-467, 1980.

The effect of 3 to 4 weeks of chronic lithium (Li) treatment in food on amphetamine-induced stereotypy, hyperactivity, and hypothermia was examined with rats. The long-term Li treatment failed to inhibit these behaviors and even resulted in small

but statistically significant potentiation of stereotypy and hypothermia. The absence of an inhibitory effect of Li on these dopaminergic processes is consistent with Li's lack of antischizophrenic properties. Reasons for conflicting results of previous studies are discussed. 40 references. (Author abstract modified)

**003153** Eckerman, David A.; Gordon, Winford A.; Edwards, Joseph D.; MacPhail, Robert C.; Gage, Michael I. Dept. of Psychology, Davie Hall 013A, University of North Carolina, Chapel Hill, NC 27514 **Effects of scopolamine, pentobarbital, and amphetamine on radial arm maze performance in the rat.** Pharmacology Biochemistry and Behavior. 12(4):595-602, 1980.

The effects of scopolamine, pentobarbital, and amphetamine on radial arm maze performance in the rat were investigated. Rats were trained to obtain food pellets from the end of each arm of an eight arm radial maze. Baseline performance was characterized by very few entries into arms from which the food pellet had already been obtained. In Experiment 1, neither d-amphetamine nor pentobarbital affected choice accuracy, although the rate of arm entry increased after d-amphetamine and decreased after pentobarbital. Scopolamine reduced both accuracy and the rate of arm entry. In a second experiment, the effects of scopolamine were replicated using a between Ss design. Methylscopolamine was found to have little effect on performance. Multiple response criteria were also compared in the second experiment. Scopolamine was found to affect runs farther out the arm differently than it affected abbreviated arm entrances. A posttrial feeding test was also included to evaluate changes in reinforcer effectiveness, and showed that food continues to be a reinforcer after both scopolamine and methylscopolamine. 34 references. (Author abstract modified)

**003154** Ehrlich, Barbara E.; Diamond, Jared M.; Braun, Leon D.; Cornford, Eain M.; Oldendorf, William H. Dept. of Physiology, UCLA School of Medicine, Los Angeles, CA 90024 **Effects of lithium on blood-brain barrier transport of the neurotransmitter precursors choline, tyrosine and tryptophan.** Brain Research. 193(2):604-607, 1980.

Brain uptake of the neurotransmitter precursors choline, tyrosine, and tryptophan was studied in lithium treated and control male Sprague-Dawley rats. Brain uptake of tyrosine and tryptophan was not affected by chronic lithium administration or an acute lithium load. However, chronic lithium treatment decreased the uptake of choline across the blood-brain barrier by 20%. 12 references.

**003155** Eichler, Alan J.; Antelman, Seymour M.; Black, Cynthia A. Antelman: Western Psychiatric Institute and Clinic, School of Medicine, University of Pittsburgh, Pittsburgh, PA 15260 **Amphetamine stereotypy is not a homogeneous phenomenon: sniffing and licking show distinct profiles of sensitization and tolerance.** Psychopharmacology. 68(3):287-290, 1980.

The sniffing and licking components of amphetamine-induced stereotypy were studied in male Sprague-Dawley rats. A gradual increase in the intensity and duration of sniffing was observed with chronic amphetamine treatment. Tolerance to the drug's effect on licking was observed during the first 3 weeks of treatment, but licking then progressively increased. Results suggest that amphetamine-induced sniffing and licking are probably subserved by distinct neuroanatomical substrates. The sensitization of sniffing behavior is discussed in relation to amphetamine-induced paranoid psychosis in humans. 25 references. (Author abstract modified)

**003156** Erickson, Carlton K.; Tyler, Thomas D.; Beck, Larry K.; Duensing, Kenneth L. College of Pharmacy, University of Texas, Austin, TX 78712 **Calcium enhancement of alcohol and drug-induced sleeping time in mice and rats.** Pharmacology Biochemistry and Behavior. 12(5):651-656, 1980.

When calcium was injected intracerebroventricularly prior to a hypnotic dose of ethanol in mice and rats, the duration of sleeping time (loss of righting reflex, LRR) was significantly enhanced. Calcium also enhanced the duration of LRR induced by t-butanol and chloral hydrate, but not that induced by sodium pentobarbital. Manganese, cadmium, and zinc also enhanced ethanol-induced LRR. Additional data suggested that a membrane associated calcium pool may be involved in the hypnotic effect of ethanol. 41 references. (Author abstract modified)

**003157** Ettenberg, Aaron; Cinsavich, Scott A.; White, Norman. Dept. of Psychology, McGill University, 1205 Docteur Penfield Avenue, Montreal, Quebec, Canada H3A 1B1 **Performance effects with repeated-response measures during pimozide-produced dopamine receptor blockade.** Pharmacology Biochemistry and Behavior. 11(5):557-561, 1979.

The effect of dopamine receptor blockade on response during extinction was investigated. Rats were trained to lever-press for either food reward or brain stimulation reward on a continuous reinforcement schedule, then extinguished under the influence of pimozide, a dopamine receptor blocking agent. Pimozide produced a dose dependent reduction in the mean number of responses to extinction made by the rates in each group. In a second experiment, pimozide produced a similar dose dependent decrease in the performance of a naturally occurring behavior that had never been associated with reward. These data suggest that dopamine receptor blockade can produce a performance deficit in situations which require repetitive responses, and that this deficit is unrelated to the presence or absence of reward. 18 references. (Author abstract modified)

**003158** Fabre-Nys, C.; Signoret, J. P. I.N.R.A., -Station de Physiologie de la Reproduction, F-37380 Nouzilly, France **Effect of cyproterone acetate on steroid-induced sexual behavior in adult ewes.** Pharmacology Biochemistry and Behavior. 12(3):359-363, 1980.

The inhibitory effect of cyproterone acetate on sexual behavior has been investigated in adult ovariectomized ewes treated with either testosterone propionate or estradiol benzoate to induce male activity and female receptivity simultaneously. Intramuscular injections of 100mg cyproterone acetate/day resulted in a rapid decrease in some of the male sexual responses after both testosterone and estradiol treatments, whereas the female reactions were eliminated by cyproterone acetate only when they had been induced by testosterone. Results are discussed in relation to three hypotheses concerning the inhibitory effects of cyproterone acetate. It is noted that cyproterone acetate seems to be less active when sexual behavior is induced by an homologous hormone than when it is induced by an heterologous hormone. 44 references. (Author abstract modified)

**003159** Fehr, Kevin OBrien; Kalant, Harold; Knox, George V. Dept. of Pharmacology, University of Toronto, Toronto, Ontario, Canada **Residual effects of high-dose cannabis treatment on learning, muricidal behavior and neurophysiological correlates in rats.** In: Nahas, G., Marihuana: biological effects. Oxford, Pergamon, 1979. 777 p. (p. 681-691).

To examine the residual effects of cannabis treatment on learning muricidal behavior, and neurophysiological correlates, immature male rats were given large oral doses of cannabis extract, ethanol, or control solution daily, for 6 months. Results show that 1 month after the end of treatment the cannabis and ethanol groups showed significantly impaired learning of a complex motor performance. In addition, a much higher proportion of the cannabis and ethanol groups showed muricidal behavior

when tested at 1 and 2 months after the end of drug treatment. These animals also showed irregular spike-like waves in electrical recordings from the dorsal hippocampus. Pilot studies suggest a reduced number of dendritic spikes in the hippocampus and cortex of the ethanol treated animals, but not in the cannabis group. In contrast, brief intrauterine exposure to comparable doses of cannabis extract during the critical phase of nervous development did not affect maze learning ability of the offspring. However, mothers were apparently able to distinguish drug treated offspring from control offspring, suggesting existence of subtle behavioral differences. 30 references. (Author abstract modified)

**003160** Fernandez-Tome, Ma Paz; Sanchez-Blazquez, Pilar; del Rio, Joaquin. del Rio: Institute of Medicinal Chemistry, C.S.I.C., Calle Juan de la Cierva 3, Madrid-6, Spain **Impairment by apomorphine of one-trial passive avoidance learning in mice: the opposing roles of the dopamine and noradrenaline systems.** Psychopharmacology. 61(1):43-47, 1979.

The effects of apomorphine on a one trial passive-avoidance learning task in mice are reported. Pretraining administration of the dopaminergic stimulant apomorphine impaired retention performance of mice on a one trial passive-avoidance task. Only with a very high dose of this drug did the effect seem related to an interference with memory formation processes. Of the dopamine receptor blocking agents used, haloperidol, but not chlorpromazine or clozapine, prevented the apomorphine effect. Phenoxybenzamine, a noradrenaline receptor blocker, antagonized the haloperidol effect and, when combined with a subeffective dose of apomorphine, impaired passive-avoidance learning. The results are interpreted in terms of the proposed inhibitory actions exerted by central noradrenaline on dopamine systems of the brain. 24 references. (Author abstract modified)

**003161** Figallo, Eduardo M.; Wingard, Lemuel B., Jr. Dept. of Pharmacology, Presbyterian-University Hospital, DeSoto at OHara Streets, Pittsburgh, PA 15213 **Effects of physostigmine, scopolamine, and mecamylamine on the sleeping time induced by ketamine in the rat.** Psychopharmacology. 61(1):59-62, 1979.

Additional insight was sought as to whether or not cholinergic pathways play a significant role in the mechanism of action of ketamine hydrochloride (Kh)-induced narcosis. Male Sprague-Dawley rats were injected i.p. with Kh, 80mg/K of bodyweight. Immediately after loss of righting reflex, scopolamine, physostigmine, and mecamylamine were administered i.p. to different groups of rats. The ketamine-induced sleeping time was significantly prolonged by physostigmine and scopolamine, but not by mecamylamine. After the delayed injection of physostigmine, the ketamine sleeping time was longer. These results, although too preliminary for a mechanistic interpretation, suggest that multiple neurotransmitter systems, probably including the cholinergic system, are involved in the mechanism of action of ketamine-induced narcosis. 24 references. (Author abstract modified)

**003162** File, Sandra E.; Clarke, Anthony. Dept. of Pharmacology, School of Pharmacy, University of London, 29/39 Brunswick Square, London WC1N 1AX, England **Intraventricular ACTH reduces social interaction in male rats.** Pharmacology Biochemistry and Behavior. 12(5):711-715, 1980.

Intracerebroventricular administration of the adrenocorticotrophic hormone fragments ACTH1-24 (1.25mcg), ACTH4-10 (1.6mcg), and ACTH4-10:D-Phe (1.6mcg) significantly reduced the time pairs of male Norway rats spent in social interaction. This decrease in social behavior was not associated with a decrease in motor activity. None of the ACTH fragments altered the latency to drink in an unfamiliar environment in thirsty rats. Possible anxiogenic actions of ACTH are discussed. 25 references. (Author abstract modified)

**003163** Fink, H.; Morgenstern, R.; Oelssner, W. Institute of Pharmacology and Toxicology, Humboldt University, Clara-Zetkin-Street 94, DDR-108 Berlin, Germany **Psychotomimetics, potentiate locomotor hyperactivity induced by dopaminergic drugs.** Pharmacology Biochemistry and Behavior. 11(5):479-482, 1979.

The influence of psychotomimetics on the increased locomotor activity of rates caused by the dopaminergic agonist, apomorphine, and the indirect sympathomimetic drug, amphetamine, was investigated in an open-field test. Apomorphine and d,l-amphetamine caused a dose dependent increase of locomotor activity. LSD, mescaline, and DMT in low doses were ineffective when given alone, but caused a strong potentiation of the hypermotility induced by apomorphine and d,l-amphetamine. Cyproheptadine antagonized the potentiating effect of LSD without affecting the hypermotility induced by apomorphine, indicating a causal serotonergic involvement in the potentiation effect. The inhibitory action of psychotomimetics at presynaptic serotonergic receptors seems to be responsible for the potentiating effect, whereas the stimulation of dopaminergic activity is a prerequisitie to the realization of this effect. 20 references. (Author abstract modified)

**003164** Fjalland, Bjarne. Department of Biology N, Royal Danish School of Pharmacy, Universitetsparken 2, DK-2100 Copenhagen O, Denmark **Neuroleptic influence on hyperthermia induced by 5-hydroxytryptophan and p-methoxy-amphetamine in MAOI-pretreated rabbits.** Psychopharmacology. 63(2):113-117, 1979.

The modulating effects of neuroleptics on 5-HT-induced hypothermia were investigated in rabbits. Some neuroleptics, piflutixol, spiroperidol and methiotepine, are extremely potent inhibitors of the induced hyperthermia. Also, the 5-HT receptor blocking agent methergoline antagonizes hyperthemia induced by the two substances in rather low doses. It is concluded that both 5-HT and catecholamine receptor blockade is required to antagonize 5-HTP hyperthermia, and that antagonism of p-MA-induced hyperthermia is primarily a result of influence on the 5-HT system. 16 references. (Author abstract modified)

**003165** Fjalland, Bjarne. Department of Biology N, Royal Danish School of Pharmacy, Universitetsparken 2, DK-2100 Copenhagen O, Denmark **Antagonism of apomorphine-induced hyperthermia in MAOI-pretreated rabbits as a sensitive model of neuroleptic activity.** Psychopharmacology. 63(2):119-123, 1979.

The effects of neuroleptics on apomorphine-induced hypothermia were investigated in rabbits. Apomorphine induced dose dependent hyperthermia in rabbits pretreated with a monoamine oxidase inhibitor. Inhibition of the synthesis of catecholamines did not influence apomorphine-induced hyperthermia, whereas 5-HT synthesis inhibition by PCPA completely abolished the hyperthermic response. Some neuroleptics and a 5-HT receptor blocking agent inhibited the hyperthermia in very low doses. A highly significant correlation was registered between the antagonism of apomorphine hypterthermia of 15 neuroleptics and their clinically useful doses. It is concluded that apomorphine-induced hyperthermia is a result of direct stimulation of dopamine receptors and release of 5-HT, and that abolition of this response represents a very sensitive in vivo model for neuroleptic substances. 21 references. (Author abstract modified)

**003166** Flemenbaum, Abraham. Louisiana State University Medical Center, PO Box 33932, Shreveport, LA 71130 **Rat dopamine hypersensitivity: I. Effect of age.** Neuropsychobiology. 5(4):213-221, 1979.

Two groups of five Sprague-Dawley rats were tested with either delta-amphetamine or saline following a drug abuse kindling model for dopaminergic hypersensitivity on pretest and posttest. However, when the animals were 40 weeks older, the saline group also received delta-amphetamine. Thus, this group served as saline control for the initial two tests and as delta-amphetamine control for age on the third session. The control group showed significantly more stereotyped behavior on phase 3 as compared with the experimental group in the first session. These results suggest an increased responsivity of dopaminergic receptors with age as measured by stereotyped behavior in rats. 38 references. (Author abstract)

**003167** Flemenbaum, Abraham. Louisiana State University Medical Center, PO Box 33932, Shreveport, LA 71130 **Rat dopaminergic hypersensitivity: II. Effects of sex.** Neuropsychobiology. 5(4):222-231, 1979.

Two groups of five male and five female Sprague-Dawley rats were tested for dopaminergic hypersensitivity on delta-amphetamine or apomorphine following a drug abuse kindling model. In contrast to the males, the female animals did not develop hypersensitivity on either drug, had a higher baseline stereotyped behavior on low doses of delta-amphetamine, and lower baseline for apomorphine. Furthermore, on apomorphine the females showed tolerance instead of hypersensitivity with a significant decrease of stereotyped behavior at posttest as compared with pretest. Female rats do not develop a readily demonstrable dopaminergic hypersensitivity with this procedure and show an absence of reverse tolerance to apomorphine. 14 references. (Author abstract)

**003168** Ford, R. D.; Rech, R. H.; Tobin, D. Center of Experimental Pathology and Toxicology, Albany Medical College, Albany, NY 12208 **Interactions between stimulants and depressants on schedule-controlled behavior.** Pharmacology Biochemistry and Behavior. 12(5):657-661, 1980.

Interactions between d-amphetamine and diazepam, d-amphetamine and methaqualone, and cocaine and diazepam were examined in daily 1 hour sessions of a fixed-interval 30 schedule of food reinforced behavior in female Sprague-Dawley rats. Results indicate that the interactions between these drug classes are complex, poorly dose related, and not predictable on the basis of the effects of the agents when given singly. Amphetamine and diazepam showed synergism or potentiation at many dose combinations. Cocaine decreased, increased, or failed to alter response rates in rats treated with diazepam, depending on the particular dose combination used. Methaqualone potentiated the increased response rate caused by d-amphetamine. 26 references. (Author abstract modified)

**003169** Freed, William J.; Perlow, Mark J.; Wyatt, Richard Jed. Laboratory of Clinical Psychopharmacology, Div. of Special Mental Health Research, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Calcitonin: inhibitory effect on eating in rats.** Science. 206(4420):850-852, 1979.

A study describing the inhibitory effects on eating in rats of subcutaneous and intracerebral injections of calcitonin, is presented. The anorectic activity of calcitonin was destroyed by exposing the hormone to heat, trypsin, or hydrogen peroxide. Calcitonin did not produce a conditioned taste aversion to saccharin, and maximum inhibition of feeding occurred 4.5 to 8.3 hours after subcutaneous administration. It is concluded that calcitonin inhibits feeding by acting directly on the CNS. 17 references. (Author abstract modified)

**003170** Frenk, Hanan; Rosen, Jeffrey B. Psychobiology Research Unit, Dept. of Psychology, Tel-Aviv University, Ramat Aviv, Israel **Suppressant effects of naltrexone on water intake in rats.** Pharmacology Biochemistry and Behavior. 11(4):387-390, 1979.

Naltrexone suppressed water intake in water deprived female Wistar rats when injected i.p. 4 hours (but not 12 hours) prior to the drinking session. In nondeprived animals, water intake and body weight were not significantly altered by i.p. injection of 5mg/kg naltrexone twice daily or by oral self-administration of naltrexone in doses sufficient to block morphine-induced analgesia. Results suggest that the suppressant effects of naltrexone on appetitive behavior are mediated by a population of opiate receptors distinct from those mediating morphine-induced analgesia. 32 references. (Author abstract modified)

**003171** Fuenmayor, Luis D.; Vogt, Marthe. Vogt: A.R.C. Institute of Animal Physiology, Babraham, Cambridge CB2 4AT, England **Production of catalepsy and depletion of brain monoamines by a butyrophenone derivative.** British Journal of Pharmacology. 67(1):115-122, 1979.

The cataleptic and monoamine depleting effects of the butyrophenone derivative 4'-fluoro-4-((4-(p-fluorophenyl)-3-cyclohexen-1-yl)-amino)-butyropheno e hydrochloride (U-32,802A) were compared to those of tetrabenazine in male albino rats and mice. Both drugs produced a dose related cataleptic state and a large reduction in the content of 5-hydroxytryptamine, dopamine, and noradrenaline in different parts of the brain, with a concomitant elevation in levels of the metabolites 5-hydroxyindol-3-yl acetic acid and homovanillic acid. The time cn ± 3 GCe catalepsy and the U-32,802A suggests the drug may act primarily at the presynaptic organelle for storage of monoamines in a way similar to tetrabenazine. 27 references. (Author abstract modified)

**003172** Fuenmayor, Luis D.; Vogt, Marthe. Vogt: ARC Institute of Animal Physiology, Babraham, Cambridge CB2 4AT, England **The influence of cerebral 5-hydroxytryptamine on catalepsy induced by brain-amine depleting neuroleptics or by cholinomimetics.** British Journal of Pharmacology. 67(2):309-318, 1979.

The involvement of 5-hydroxytryptamine (5-HT) in the catalepsy induced by tetrabenazine or the butyrophenone U-32,802A in male albino rats and mice was examined. Pretreatment with p-chlorophenylalanine (PCPA) reduced the intensity of catalepsy induced by the neuroleptics by 50% or more without altering its duration. The neuroleptic-induced catalepsy was enhanced by 5-hydroxytryptophan (5-HTP) when given 45 minutes, but not 90 minutes, after the neuroleptic. The anticataleptic effect of PCPA was reversed by 5-HTP. The modification of catalepsy by 5-HTP and PCPA was accompanied by measurable changes in 5-HT metabolism in the rat forebrain. Pretreatment with methysergide reduced the neuroleptic-induced catalepsy in both species and prevented the enhancing effects of 5-HTP. Tryptophan increased neuroleptic-induced catalepsy in mice and increased the production of 5-hydroxyindol-3-ylacetic acid in the forebrain. Catalepsy induced by central administration of physostigmine in rats was not altered by methysergide or PCPA, but was abolished by atropine. In mice, catalepsy induced by systemic pilocarpine was abolished by atropine and not altered by methysergide or 5-HTP. Results suggest that serotonergic neurons are involved in facilitating neuroleptic-induced catalepsy. 27 references. (Author abstract modified)

**003173** Fujiwara, Michihiro; Ibii, Nobuhiro; Kataoka, Yasufumi; Ueki, Showa. Ueki: Dept. of Pharmacology, Faculty of Pharmaceutical Sciences, Kyushu University, Fukuoka 812, Japan **Effects of psychotropic drugs on delta9-tetrahydrocannabinol-induced long-lasting muricide.** Psychopharmacology. 68(1):7-13, 1980.

The effects of psychotropic drugs on the long lasting muricide induced in male Wistar King-A rats by delta9-tetrahydrocannabinol (THC) were examined. THC-induced muricide was inhibited by all drugs tested. Atropine, antiparkinsonism drugs, and imipramine-like antidepressants selectively inhibited muricide, without altering open-field behavior. Neuroleptics, pentobarbital, diazepam, and methamphetamine had nonspecific effects. THC-induced muricide may be a useful model for evaluating antidepressant drugs. 29 references. (Author abstract modified)

**003174** Fung, Yiu K.; Uretsky, Norman J. Uretsky: Division of Pharmacology, College of Pharmacy, Ohio State University, Columbus, OH 43210 **Effect of calcium on locomotor activity in mice.** Psychopharmacology. 68(2):207-208, 1980.

Intracerebroventricular administration of calcium severely depressed the locomotor activity of unanesthetized Male CD1 mice, producing ataxic gait and motor incoordination. Pretreatment with pentobarbital (30mg/kg i.p.) twice daily for 2 or 6 days partially reversed the effect of calcium. Results suggest that calcium and pentobarbital may exert their depressant effects through similar mechanisms. 7 references. (Author abstract modified)

**003175** Furukawa, Tatsuo; Yamada, Katsushi. Yamada: Dept. of Pharmacology, School of Medicine, Fukuoka University, Fukuoka 814, Japan **The alpha-naphthoxyacetic acid-elicited retching involves dopaminergic inhibition in mice.** Pharmacology Biochemistry and Behavior. 12(5):735-738, 1980.

Alpha-naphthoxyacetic acid (alpha-NOAA) elicited a dose dependent retching behavior at doses from 250 to 550mg/kg in ddY male mice and induced vomiting at a dose of 550mg/kg in pigeons. Protoveratrine-A (PV-A, 0.1mg/kg), a veratrum alkaloid, also induced retching in mice and vomiting in pigeons. Apomorphine (2mg/kg) markedly inhibited the retching elicited by alpha-NOAA or PV-A. The inhibitory effects of apomorphine were antagonized by haloperidol, but the antagonism was not significant. Scopolamine, aminooxyacetic acid, and gamma-butyrolactone did not significantly affect the retching elicited by alpha-NOAA or PV-A. Results suggest that dopaminergic inhibition is involved in the retching elicited by alpha-NOAA or PV-A. 14 references. (Author abstract modified)

**003176** Gallagher, Michela; Kapp, Bruce S.; Frysinger, Robert C.; Rapp, Peter R. Dept. of Psychology, University of Vermont, Burlington, VT 05405 **Beta-adrenergic manipulation in amygdala central n. alters rabbit heart rate conditioning.** Pharmacology Biochemistry and Behavior. 12(3):419-426, 1980.

The effects of beta-adrenergic manipulation within the central nucleus of the amygdala on Pavlovian heartrate conditioning in the rabbit were investigated. Administration of the beta-adrenergic antagonist dl-propranolol into the central nucleus impaired the acquisition of conditioned heartrate responding compared to a vehicle injected control group. No significant effects of dl-propranolol on either baseline heartrate or on the heartrate orienting response were observed. The effect of dl-propranolol on conditioning exhibited stereospecificity, and animals receiving combined intracerebral injections of dl-propranolol and the beta-adrenergic agonist l-isoproterenol did not exhibit comparable conditioning impairments. In addition, dl-propranolol administration dorsal to the central nucleus or into amygdala sites anterior or posterior to the central nucleus was less effective. These results support the interpretation that beta-adrenergic activity within the central nucleus region of the amygdala complex contributes to the acquisition of classically conditioned heartrate responding. 34 references. (Author abstract)

**003177** Gessner, Peter K.; Clarke, Carolyn C. Dept. of Pharmacology and Therapeutics, State University of New York at Buffalo, Buffalo, NY 14214 **Effects of meperidine on operant behavioral thermoregulation in mice under conditions of symmetrical thermal drive.** Psychopharmacology. 65(1):59-63, 1979.

The effects of meperidine on operant behavioral thermoregulation were investigated using a convective thermal controller and mice trained to alternate at will the thermal drive condition, changing it from an air flow of 15 degrees C to one of 45 degrees C, and vice versa. Administration of 15 mg/kg meperidine resulted in significantly lower response rates, a significantly larger fraction of time spent in one (mostly cold) drive condition, and significantly lower body temperatures than administration of saline. In a second experiment, the animal was automatically returned to the hot drive condition every 3 min unless it had been exposed to this condition in the previous 0.4 min although otherwise it remained free to alternative drive conditions at will. Under these conditions, meperidine treated animals also spent significantly more time in cold drive and had significantly lower body temperatures than control animals, in spite of lower response rates. Pretreatment with 4.5 mg/kg tranylcypromine (4 h prior) did not significantly alter the effects of meperidine administration in either experiment. 19 references. (Author abstract)

**003178** Geyer, Mark A.; Light, Roger K.; Rose, Gary J.; Petersen, Lyle R.; Horwitt, David D.; Adams, Lynne M.; Hawkins, Richard L. Dept. of Psychiatry, UCSD School of Medicine, La Jolla, CA 92093 **A characteristic effect of hallucinogens on investigatory responding in rats.** Psychopharmacology. 65(1):35-40, 1979.

The effects of a variety of hallucinogens as well as several representatives of disparate drug classes on investigatory responding in rats were investigated. The disruption of the temporal distribution of investigatory responses by rats in a novel hole board following LSD was found to be a characteristic effect of a variety of hallucinogens. Similar effects were produced by indoleamine hallucinogens and by phenylethylamine hallucinogens. Congeners of 2,5-dimethoxy-4-methylamphetamine that are inactive in humans had no significant effects. Of a variety of other psychoactive drugs tested, only apomorphine produced an effect similar to that of hallucinogens. The results suggest that a simple behavioral measure of exploration in a hole board may provide a useful animal model with which to examine the common effects of hallucinogens. 26 references. (Author abstract modified)

**003179** Geyer, Mark A.; Light, Roger K. Dept. of Psychiatry, UCSD School of Medicine, La Jolla, CA 92093 **LSD-induced alterations of investigatory responding in rats.** Psychopharmacology. 65(1):41-47, 1979.

The effects of lysergic acid diethylamide (LSD) on investigatory responses of rats in a novel hole board were assessed. LSD altered the temporal distribution of nose poke responses during a 24 min session; LSD treated rats responded less than controls initially, yet increased their response rates late in the session. When handling stress was minimized by placing the animals in an anteroom for 10 min before starting the test, the distribution of responding was normal although the overall frequency was still reduced. Conversely, vigorous handling potentiated the LSD effect. The results are interpreted as indicating an increased sensitivity of the LSD treated rats to the stimuli associated with being handled and placed into the novel hole board rather than a direct effect on investigatory tendencies. This LSD-induced potentiation of defensive responses appears to compete with the active exploration of the novel environment. 31 references. (Author abstract modified)

**003180** Gianutsos, G.; Moore, K.E. School of Pharmacy, University of Conneticut, Storrs, CT 06268 **Differential behavioral and biochemical effects of four dopaminergic agonists.** Psychopharmacology. 68(2):139-146, 1980.

The dopaminergic agonists apomorphine, piribedil, lergotrile, and bromocriptine all caused a dose dependent reversal of the alpha-methyltyrosine-induced decline of forebrain dopamine (DA) in male Swiss-Webster mice. All four compounds reduced locomotor activity at low doses, but only apomorphine and bromocriptine increased motor activity at high doses. Chronic treatment with haloperidol altered the effects of lergotrile and bromocriptine. Results suggest that dopaminergic agonists may interact with more than one population of DA receptors. 38 references. (Author abstract modified)

**003181** Gianutsos, Gerald. Dept. of Pharmacology, University of Connecticut, Storrs, CT 06268 **Altered pilocarpine- or chlorpromazine-induced catalepsy after long-term treatment with cholinergic drugs.** Psychopharmacology. 66(2):121-125, 1979.

The interaction effects of dopamine receptor blockers and cholinergic agonists after prolonged manipulation of cholinergic receptors was investigated in mice. Long-term administration of the cholinergic drug pilocarpine attenuated the catalepsy induced by an acute injection of pilocarpine or the dopamine antagonist chlorpromazine. Similar results (i.e., tolerance to pilocarpine and cross-tolerance to chlorpromazine) were noted in mice chronically treated with the cholinesterase inhibitor physostigmine but not in mice chronically treated with neostigmine, a cholinesterase inhibitor which does not penetrate the central nervous system. Mice maintained on the anticholinergic scopolamine showed the opposite effect; there was an increase in the sensitivity to the catalepsy induced by pilocarpine or chlorpromazine. The results suggest that long-term changes in cholinergic receptors may indirectly alter the behavioral effects of drugs which act via dopamine. 28 references. (Author abstract modified)

**003182** Giles, H. G.; Kadar, G.; MacLeod, S. M.; Sellers, E. M. Clinical Pharmacology Program, Clinical Institute, Addiction Research Foundation, Toronto, Ontario, Canada M5S 2S1 **Use of the overturn end point in goldfish to measure the interaction of diazepam and ethanol and the effects of the binding of diazepam to bovine serum albumin.** Canadian Journal of Physiology and Pharmacology. 57(10):1186-1188, 1979.

The interaction of diazepam and ethanol was studied in goldfish by determining the doses at which the fish failed to right itself within 1 to 2 seconds after being turned over with a glass rod. The effects of the two agents on the overturn endpoint were additive over a range of 0.000028 to 0.0000878M diazepam and 0.0485 to 0.0122M ethanol. The addition of 0.0000156 bovine serum albumin to aqueous solutions of diazepam modified the diazepam effect by reducing the free drug concentrations. It is concluded that the overturn endpoint test in goldfish may be a useful means of predicting drug interactions with ethanol. 7 references. (Author abstract modified)

**003183** Glennon, Richard A.; Young, Richard; Rosecrans, John A.; Kallman, Mary J. Dept. of Pharmaceutical Chemistry, School of Pharmacy, Virginia Commonwealth University, Richmond, VA 23298 **Hallucinogenic agents as discriminative stimuli: a correlation with serotonin receptor affinities.** Psychopharmacology. 68(2):155-158, 1980.

Sprague-Dawley rats were trained to discriminate 5-methoxy-N,N- dimethyltryptamine (5-OMeDMT) from saline in a two lever choice task under a variable interval 15 second of sweetened milk reinforcement. The 5-OMeDMT stimulus generalized in a dose dependent manner to each of 14 tryptamine related analogs. The effective dose for the 5-OMeDMT response correlated highly with the serotonin receptor affinity of all but one of the analogs. 20 references. (Author abstract modified)

**003184** Gold, Paul E.; Reigel, Judith A. Dept. of Psychology, Gilmar Hall, University of Virginia, Charlottesville, VA 22901 **Extended retrograde amnesia gradients: peripheral epinephrine and frontal cortex stimulation.** Physiology & Behavior. 24(6):1101-1106, 1980.

The effects of hormonal responses to training on the susceptibility of memory to an amnestic agent were studied in male Sprague-Dawley rats. Rats trained on a one trail passive avoidance response and, up to one week later, given a subcutaneous injection of epinephrine shortly before electrical stimulation of frontal cortex exhibited amnesia on retention tests. Results suggest that neuroendocrine responses to training may potentiate the effects of amnestic agents on memory. 43 references. (Author abstract modified)

**003185** Golus, Peter; McGee, Rob. Dept. of Psychology, University of Newcastle, Newcastle, New South Wales 2308, Australia **Metrazol produces conditioned taste aversion in rats.** Psychopharmacology. 68(3):257-259, 1980.

he convulsant drug metrazol produced a conditioned taste aversion to saccharin in a two bottle preference test in male Wistar rats. This finding contradicts previous reports and highlights the sensitivity of the two bottle method for detecting taste aversion. Saccharin intake was suppressed in both convulsed and nonconvulsed animals, indicating the aversive effect of metrazol was not dependent on production of convulsions. 7 references. (Author abstract modified)

**003186** Gonzalez Perez, Jose N.; Gonzalez-Quevedo, Alina. Instituto de Neurologia y Neurocirugia, Calle 29 y D, Vedado, Havana, Cuba **Blockade of audiogenic seizures by bromocryptine.** Pharmacology Biochemistry and Behavior. 12(5):823-825, 1980.

Bromocriptine (5mg/kg) greatly reduced the incidence and lethality of audiogenic seizures in 21-day-old DBA/2H mice. This effect increased with time during the first hour after injection. Pretreatment with spiroperidol (0.5mg/kg) blocked the protective effect of bromocriptine. Results suggest that dopaminergic pathways are involved in inhibition of audiogenic seizures. 21 references. (Author abstract modified)

**003187** Gordon, John H.; Gorski, Roger A.; Borison, Richard L.; Diamond, Bruce I. Dept. of Pharmacology, Chicago Medical School, Chicago, IL **Postsynaptic efficacy of dopamine: possible suppression by estrogen.** Pharmacology Biochemistry and Behavior. 12(4):515-518, 1980.

The effects of estrogen treatment on the efficacy of apomorphine in developing stereotyped behavior in the rat were evaluated. Treatment of ovariectomized rats with estradiol benzoate (EB) prior to testing for stereotyped behavior shifted the dose response curve for apomorphine to the right, increasing the median effective dose from 0.38 to 0.65mg/kg. Ovariectomized rats treated chronically with EB for 14 days were more responsive than oil injected controls when challenged with apomorphine on the seventh day after cessation of EB treatment. Similarly long-term ovariectomized rats also display an enhanced response to apomorphine in terms of development of stereotyped behavior. The reduced response to apomorphine following acute EB (3 days) can be interpreted as a possible decrease in either the number or affinity of dopamine receptors. Moreover, the enhanced response to apomorphine after cessation of chronic EB treatment (14 days) may be explained on the basis of a decrease in the postsynaptic efficacy of dopamine during chronic treatment with EB, which is then overcompensated for upon with-

drawal from chronic treatment. The increased sensitivity to apomorphine in long-term ovariectomized animals is also consistent with the chronic suppression of dopamine efficacy in the intact female animal. 32 references. (Author abstract modified)

**003188** Gorka, Z.; Ossowska, K.; Stach, R. Institute of Pharmacology, Polish Academy of Sciences, Krakow, Poland **The effect of unilateral amygdala lesion on the imipramine action in behavioural despair in rats.** Journal of Pharmacy and Pharmacology. 31(9):647-648, 1979.

The effects of imipramine on performance in the behavioral despair test were examined in male Wistar rats with unilateral lesions of the basolateral nuclei of the amygdaloid complex and in control and sham-operated rats. Imipramine reduced the immobility induced by forced swimming in all three groups, but the effect was significantly decreased in the lesioned group. This finding suggests that the amygdala may be the site of the antidepressant action of imipramine. 9 references.

**003189** Graeff, F. G.; Leone, C. M. L. Dept. of Experimental Psychology, University of Oxford, South Parks Road, Oxford OX1 3UD, England **Effect of amphetamine on nondiscriminated key-pecking avoidance in pigeons.** Psychopharmacology. 61(1):91-96, 1979.

Dose effect curves for amphetamine on keypecking behavior of pigeons maintained by two component multiple schedules of shock postponement were determined. During the first phase response/shock interval (RS) was held constant and the shock/shock interval (SS) varied. Shock rate was greater during the shorter SS. In the second phase SS was held constant while RS varied. Baseline response rate was considerably lower when the RS was longer. The effects of amphetamine in the two schedule components were markedly different, lower response rates being considerably more increased than higher rates. 18 references. (Author abstract modified)

**003190** Grecksch, Gisela; Matthies, Hansjurgen. Institute of Pharmacology and Toxicology, Medical Academy, 301 Magdeburg, Germany **Two sensitive periods for the amnesic effect of anisomycin.** Pharmacology Biochemistry and Behavior. 12(5):663-665, 1980.

Anisomycin impaired retention of a brightness discrimination in rats when the drug (80mcg) was injected bilaterally into the hippocampi 10 minutes before and 80 minutes after training or 240 and 360 minutes after training. No amnesia was observed when anisomycin was given 45 and 165 minutes after training. The two separate sensitive periods for the amnesic effect of the inhibitor appeared to correspond to two phases of increased protein synthesis during the consolidation of the learning procedure. 19 references. (Author abstract modified)

**003191** Green, A. R.; Bloomfield, M. R.; Atterwill, C. K.; Costain, D. W. MRC Clinical Pharmacology Unit, Radcliffe Infirmary, Oxford OX2 6HE, England **Electroconvulsive shock reduces the cataleptogenic effect of both haloperidol and arecoline rats.** Neuropharmacology. 18(5):447-451, 1979.

The cataleptic response to haloperidol (1.5mg/kg i.p.) was measured in male Sprague-Dawley rats at various times after a single daily electroconvulsive shock (ECS) for 1, 5, or 10 days or after a single daily subconvulsive shock for 10 days. The cataleptic response to haloperidol was markedly attenuated 24 (but not 48 or 12 hours after one ECS treatment, up to 48 hours after the 5 day ECS treatment, and 72 (but not 168) hours after the 10 day ECS treatment. The reduction in the cataleptic response to the cholinomimetic drug arecoline was also seen following the 1 and 10 day ECS treatments, and the time course of these changes ws similar to that observed with haloperidol. These findings are discussed in relation to the enhanced monoaminergic behavioral responses seen in rats after ECS and to the therapeutic mechanisms of electroconvulsive shock therapy. 31 references. (Author abstract modified)

**003192** Green, A. R.; Deakin, J. F. W. MRC Clinical Pharmacology Unit, Radcliffe Infirmary, Oxford OX2 6HE, England **Brain noradrenaline depletion prevents ECS-induced enhancement of serotonin-and dopamine-mediated behaviour.** Nature. 285(5762):232-233, 1980.

The effects of brain noradrenaline depletion on the electroconvulsive shock (ECS) induced enhancement of serotonin and dopamine mediated behavior were investigated in rats. Destruction of brain noradrenergic systems totally abolished the ability of ECS to potentiate quipazine and apomorphine-induced hyperactivity. Results demonstrate that noradrenaline is not involved in the mediation of the behavioral syndromes themselves, as the lesion was without effect in nonshocked animals. The data suggest that changes occur in brain noradrenergic systems during ECS that result in enhancement od serotonin and dopamine mediated behavior. The relationship between these results and the antidepressant action of electroconvulsive therapy is discussed. 22 references. (Author abstract modified)

**003193** Grieve, Susan J.; Littleton, John M. Dept. of Pharmacology, King's College, Strand, London WC2R 2LS, England **The rapid development of functional tolerance to ethanol by mice.** Journal of Pharmacy and Pharmacology. 31(9):605-610, 1979.

The development of functional tolerance to ethanol was examined in adult male TO Swiss mice during inhalation of ethanol vapor. Peak tolerance developed within 3 to 5 hours; at this point, the blood ethanol concentration required to produce loss of righting reflex or rotorod balance was about twice that needed in naive mice. The ability of the animals to perform normally in the presence of continued high concentrations of ethanol in blood then began to fall. Results are discussed in relation to current concepts of tolerance to central nervous system depressant drugs. 17 references. (Author abstract modified)

**003194** Gunion, Mark William. Iowa State University **Pituitary beta-endorphin levels and naloxone effects on feeding in several experimental obesity syndromes.** Dissertation Abstracts International. 40(12):5862-B, 1980. Ann Arbor, Univ. Microfilms No. 8012962, 90p., 1980.

The effects of the opiate antagonist naloxone on feeding behavior and the measurement of pituitary beta-endorphin-like immunoreactivity were tested for each of several animal models of obesity. Adult female rats received veutromedial hypothalamic lesions (VMH), dorsolateral tegmental lesions (DLT), parasagittal hypothalamic knife cuts (KC), intra-ventricular injections of 5,7-dihydroxgytyptamine (5,7-DHT), or control surgery (NWRA), or mere ovariectomized (OVX). All animals were maintained at normal body weight during testing except for an additional group of neurologically intact rats that was maintained at 75% of normal body weight (DEP). The effect of 0.5, 1.8, 6.8, and 25.0mg/kg naloxone on the consumption of laboratory pellets was measured during 4 hr daily access periods. Results indicate that: 1) at lean body weights, feeding in the hyperphagia/obesity syndromes tested is not more or less sensitive to naloxone than in normal rats; 2) elevated concentrations of beta-endorphin-like immunoreactivity are not related to hyperphagia in the syndrome examined; and 3) obesity itself may have little if any effect on pituitary beta-endorphin-like immunoreactivity. (Journal abstract modified)

**003195** Gutwein, Baruch M.; Shiromani, Priyattam J.; Fishbein, William. Psychobiology Laboratory, Dept. of Psychology, City College of City University of New York, New York, NY **Para-**

**doxical sleep and memory: long-term disruptive effects of anisomycin.** Pharmacology Biochemistry and Behavior. 12(3):377-384, 1980.

The effects of the protein synthesis inhibitory anisomycin (ANI) on paradoxical sleep (PS or REM sleep), slow-wave sleep (SWS), and retention of one trial inhibitory avoidance training was examined in mice in three separate experiments. In Experiment 1, mice injected with ANI (120mg/kg and 210mg/kg) exhibited reductions in PS for 9 consecutive hours and ANI 40mg/kg treated mice for 6 consecutive hours with no PS rebound in all three groups. ANI increased SWS commencing 3 hr postinjection, containing for 9 consecutive hours and then returning to saline control levels. There were no significant differences between ANI treated groups in the degree of SES augmentation. In Experiment 2, the higher doses of ANI, but not the lower dose impaired retention measured 72 hr after training and induced amnesia from 3 to 9 hr posttraining. In Experiment 3, the gradient of memory trace susceptibility to disruption by electroconvulsive shock (ECS) was extended to 3 hr posttraining in mice given immediate posttraining injections of ANI 40mg/kg. ANI 20mg/kg and ANI 10mg/kg alone or in combination with ECS was ineffective in extending the lability of the memory trace. Results indicate that PS in the 3 hr period after aversively motivated training is not essential for memory processing. It is suggested that memory stability and maintenance is dependent on PS occurring over a protracted time period. 29 references. (Author abstract modified)

**003196** Gyorgy, L. Institute of Experimental Medicine, Hungarian Academy of Sciences, 1450 Budapest, P.O.B. 67, Hungary **Role of dopaminergic and GABA-ergic interactions in seizure susceptibility.** Archives Internationales de Pharmacodynamie et de Therapie. 241(2):280-286, 1979.

The interaction of dopamine and GABA containing neurons in the regulation of seizure susceptibility was examined in CFLX mice. Apomorphine and piribedil decreased seizure susceptibility to electroshock, and these effects were reduced by haloperidol. When given alone, small doses of haloperidol increased and high doses decreased seizure threshold. Amino-oxyacetic acid elevated seizure threshold; this effect was reduced by picrotoxin, haloperidol, and reserpine, but not by apomorphine. 12 references. (Author abstract modified)

**003197** Haber, Suzanne Naomi. Stanford University **The effects of amphetamine on social and individual behaviors of rhesus macaques. (Ph.D. dissertation).** Dissertation Abstracts International. 39(12):5841-B, 1979. Ann Arbor, Univ. Microfilms No. 7912366, 145p., 1979.

The effects of amphetamine on the individual and social behaviors of rhesus macaques were examined in two established colonies of monkeys (n=8). Each drug and each baseline period lasted 3 weeks. Initial doses began at 0.1mg/kg, which were increased 0.1mg/kg daily during the first week; subsequent increases depended on the ability of the animal to tolerate the drug. Results indicate that amphetamine caused significant decreases in time spent eating and huddling/sleeping during the period of drug administration only. There were no consistent changes across animals in exploring, self-grooming, or pacing behaviors. There were dramatic decreases in the sit idle, watching others calmly, and increases in sit tense and orient categories. The average distance between an animal receiving amphetamine and other colony members did not increase. However, individual relationships indicate that drug treated animals maintained closer contact with one individual, while moving further away or having less contact with other animals. Finally, agonistic encounters were found to dramatically increase during drug periods: dominant animals increased their threatening during treatment; subordinates their submissive responses. Other results suggest interesting changes in affiliative behaviors. (Journal abstract modified)

**003198** Haigler, Henry J.; Spring, Denise D. Dept. of Pharmacology, Emory University, Atlanta, GA 30322 **Drugs that antagonize limb flick behavior induced by D-lysergic acid diethylamide (LSD) in cats.** Psychopharmacology. 64(1):31-34, 1979.

The effects of four different classes of drugs on D-lysergic acid diethylamide (LSD)-induced limb flick (LF) (a sensitive measure of the behavioral effects of LSD) was examined in cats observed in their home cages. LF induced by 50 micrograms/kg LSD was blocked by dextrorphan (.6mg/kg), dextromethorphan (.6mg/kg), and imipramine (5mg/kg) at doses that did not produce ataxia or sleep. Levorphanol (.6mg/kg), a narcotic that is a cogenor of dextrorphan, did not block LSD-induced LF, possibly because it produced an excitatory effect when given alone. Pentobarbital at low doses (2 and 4mg/kg) increased the number of LFs induced by LSD, but at a high dose (8mg/kg) decreased LF either by producing ataxia, so that cats tended to remain immobile, or by producing sleep. Chlorpromazine at three doses (2, 4, and 8mg/kg) attenuated the effects of LSD on LF, but did not block LF as completely as the above three blocking drugs, and produced ataxia and sleep. Possible serotonergic mechanisms for the observed blocking effects of dextrorphan, dextromethorphan, and imipramine are discussed. 15 references. (Author abstract modified)

**003199** Hammond, Donna L.; Proudfit, Herbert K. Dept. of Pharmacology, College of Medicine, University of Illinois, Chicago, IL 60680 **Effects of locus coeruleus lesions on morphine-induced antinociception.** Brain Research. 188(1):79-91, 1980.

Nociceptive threshold and morphine analgesia were measured in female Sprague-Dawley rats after monosodium-L-glutamate lesions of the locus coeruleus (LC) and adjacent tegmentum (nucleus parabrachialis ventralis, PBV). Nociceptive thresholds were not altered by lesions of the PBV or lesions of the PBV and LC. Morphine analgesia was attenuated by lesions of the PBV alone or lesions including the PBV and LC. Lesions of the LC altered norepinephrine content in the cortex, spinal cord, and medial brainstem, but these changes could not be correlated with attenuation of morphine analgesia. Results suggest that destruction of the PBV was responsible for the attenuation of morphine analgesia. 56 references. (Author abstract modified)

**003200** Handley, Sheila L.; Thomas, Karin V. Pharmacological Laboratories, Dept. of Pharmacy, University of Aston, Birmingham B4 7ET, England **Potentiation of startle response by d- and l-amphetamine: the possible involvement of pre- and postsynaptic alpha-adrenoreceptors and other transmitter systems in the modulation of a tactile startle response.** Psychopharmacology. 64(1):105-111, 1979.

The tactile startle response to a metered puff of air was investigated in mice treated with d-amphetamine (d-amp) and l-amphetamine (l-amp) and a range of drugs acting on central transmitter systems. d-Amp produced a dose related increase in startle response amplitude (SRA), l-amp was twice as potent, and apomorphine was without effect. Noradrenaline (NA) and alpha-methyl NA intracerebroventricularly (icv), and clonidine intraperitoneally (ip), all tended to reduce control SRA but potentiated the effect of d-amp. Apomorphine ip had no effect on control SRA or on the effect of d-amp. Phenoxybenzamine, phentolamine, and piperoxane reduced d-amp potentiation at dosages which had no effect on control SRA. Higher doses of phenoxybenzamine and phentolamine reduced control SRA. Yohimbine enhanced the effect of d-amp, but reduced control SRA. dl-Propranolol, d-propranolol, and sotalol (MJ 1999) did



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not affect d-amp potentiation. Pimozide was without effect on control SRA, but caused late potentiation of the d-amp effect. H44/68 and FLA-63 reduced d-amp potentiation. Both 5-hydroxytryptamine (5-HT) icv and p-chlorophenylalanine potentiated the d-amp effect. The predominant effect of arecoline, physostigmine, and carbachol was also to potentiate the d-amp effect. Atropine and hyoscine reduced d-amp potentiation. Results are discussed in terms of involvement in the startle response of noradrenergic synapse possessing receptors resembling peripheral presynaptic and postsynaptic alpha-adrenoreceptors. Cholinergic and 5-HT systems may also be involved. 26 references (Author abstract modified)

**003201** Harrison, Paul C.; Sofia, R. Duane; Ciofalo, Vincent B. Boehringer Ingelheim, Ltd., Dept. of Pharmacology, 175 Briar Ridge Road, Ridgefield, CT 06877 **Effects of delta9-tetrahydrocannabinol (THC) on conditioned avoidance responding in mice and rats and the one-trial conflict test in rats.** Bulletin of the Psychonomic Society. 15(4):207-210, 1980.

The effects of delta9-tetrahydrocannabinol (THC) on conditioned avoidance respoding in mice and rats and the one trial conflict test in rats were examined. When administered orally to mice, 100mg/kg THC produced an increase in avoidance performance. A lower dose, 50mg/kg demonstrated a slight decrease in avoidance performance in mice. In rats, THC produced an increase at 25mg/kg and a decrease at 100mg/kg. A dose of 8mg/kg i.p. of THC produced an increase in the mean number of shocks taken by rats in the one trial conflict test. It is concluded that when evaluated with respect to neurotoxic activity as measured in the rotarod test, these data are suggestive of some (Author abstract modified)

**003202** Hecht, Arthur; Schiorring, Erik. Psychopharmacological Research Laboratory, Dept. E, Sct. Hans Hospital, DK-4000 Roskilde, Denmark **Behavioral effects of low and high acute doses of morphine in solitary mice.** Psychopharmacology. 64(1):73-79, 1979.

The effects of low and high acute doses of morphine (5, 10, 100, 150mg/kg subcutaneously) on locomotor activity, object manipulation, grooming, rearing, and responsiveness to social stimulation were observed in naive nontolerant solitary mice. Morphine induced significant changes in the behavior elements recorded. Low doses (5 and 10mg/kg)caused an initial phase of about 1 hr with inhibition of all activities. After 1 hr, the mice gradually increased activity and exceeded the corresponding placebo level at the end of the sessions. High doses (100 and 150mg/kg) caused an increase in locomotor activity. This hyperactive continuous running was stereotyped, restricted as it was to only a certain part of the experimental cage. Concurrently, all other behavior elements were abolished. The animals did not normalize within the observation period. Neither the sedated animals with low doses nor the animals with high doses of morphine responded socially to the presence of another untreated mouse which was placed in the cage as a social response test. 20 references. (Author abstract)

**003203** Hennessy, John W.; Smotherman, William P.; Levine, Seymour. Smotherman: Dept. of Psychology, Oregon State University, Corvallis, OR 97331 **Investigations into the nature of the dexamethasone and ACTH effects upon learned taste aversion.** Physiology & Behavior. 24(4):645-649, 1980.

The effects of dexamethasone and ACTH upon learned taste aversion are described. It is noted that dexamethasone injected prior to the conditioning trial attenuates a learned taste aversion, and that ACTH injections prolong the recovery from a taste aversion when admininsterd prior to recovery trials. In Experiment I, the interaction between these effects was studied. Using a factorial design, four groups of rats received dexamethasone or ACTH prior to conditioning and prior to recovery trials. An additional group received isotonic saline throughout training and recovery. The primary finding was that animals receiving dexamethasone prior to conditioning and ACTH prior to recovery trials did not differ from the group pretreated with ACTH during both conditioning and recovery. That is, given the parameters of these experiments, the ACTH effect was prepotent. In the second experiment, it was shown that the ACTH effect upon the performance of a taste aversion can occur in one trial. Taken together, results support the idea that ACTH influences memory retrieval when administered prior to a test for retention of an avoidance response. 21 references. (Author abstract modified)

**003204** Hennig, Charles W. Division of Science and Mathematics, Centre College of Kentucky, Danville, KY 40422 **Biphasic effects of serotonin on tonic immobility in domestic fowl.** Pharmacology Biochemistry and Behavior. 12(4):519-523, 1980.

In two experiments, groups of 2 1/2 to 3-week-old chickens were injected intravenously with various doses of serotonin and tested for tonic immobility. Relatively low doses of serotonin produced significant increased in the duration of tonic immobility, while high doses only produced slight decreases in duration. Serotonin also reduced the activity levels of chickens before testing for immobility and made the response easier to induce, but there were not apparent differences due to dosage for either of these behaviors. The effects by serotonin on the immobility response and activity level were found to persist for over 2 hours with little decrease in their potency. The data are discussed in relation to the contradictory effects demonstrated in previous research and in rlation to the importance of differential responding by prey during predatory encounters. 28 references. (Author abstract modified)

**003205** Hennig, Charles W.; Dunlap, William P.; Harston, Craig T.; MacPhee, Alan A. Division of Science and Mathematics, Centre College of Kentucky, Danville, KY 40422 **Tonic immobility and the alpha-adrenergic system in chickens.** Physiology & Behavior. 24(1):21-25, 1980.

The duration of tonic immobility induced by restraint in Production Red chickens was significantly decreased by the low potency alpha-adrenergic agonists methoxamine and phenylephrine and increased by the more potent alpha-adrenergic agonists norepinephrine, methyldopa, clonidine, and epinephrine. Isoproterenol, a beta-adrenergic agonist, had no apparent effect on immobility. Results indicate that the alpha-adrenergic system is involved in the immobility response.

**003206** Hennig, Charles W.; Harston, Craig T.; Dunlap, William P.; Hill, Elizabeth M.; McNichols, Michael D. Division of Science and Mathematics, Centre College of Kentucky, Danville, KY 40422 **The effects of serotonin metabolites on tonic immobility in chickens (Gallus gallus): dose and time response curves.** Physiological Psychology. 8(1):65-71, 1980.

The effects of melatonin and 5-hydroxyindoleacetic acid (5-HIAA) on tonic immobility (TI) in chickens were examined after several different postinjection time periods. Both of these metabolic byproducts of serotonin produced increases in duration of TI at 10 min postinjection, but melatonin was much more potent than 5-HIAA. In addition, melatonin produced a decrease in the duration of TI at 120 min. These results are discussed in terms of possible neurotransmitters and a central feedback system between brain levels of serotonin, its metabolites, and duration of TI. 36 references. (Author abstract)

**003207** Hill, S. Y.; Reyes, R. B.; Kupfer, D. J. Dept. of Psychiatry, University of Pittsburgh School of Medicine, Western Psy-

chiatric Institute and Clinic, Pittsburgh, PA **Physostigmine induction of REM sleep in imipramine treated rats.** Communications in Psychopharmacology. 3(4):261-266, 1979.

Sleep EEG recordings were obtained in rats administered either physostigmine alone, imipramine alone, or physostigmine plus imipramine to investigate whether the anticholinergic effects of imipramine are responsible for the drug's prolongation of REM induction. Physostigmine, a cholinesterase inhibitor, was administered in conjunction with imipramine to determine if the increased latency to REM seen with imipramine could be blocked with physostigmine, and further, to determine if other REM parameters would be similarly affected. Injection of physostigmine (1mg/kg) blocked the effects of imipramine (5mg/kg) on REM latency without affecting the percentage of REM or the number of REM episodes. Thus, the anticholinergic properties of imipramine appear to be responsible for its effect on REM induction but not maintenance of REM sleep. 17 references. (Author abstract modified)

**003208** Hirose, K.; Matsushita, A.; Kojima, Y.; Eigyo, M.; Jyoyama, H.; Shiomi, T.; Tsukinoki, Y.; Hatakeyama, H.; Matsubara, K. Division of Pharmacology, Shionogi Research Laboratory, Shionogi & Co., Ltd., Fukushima-ku, Osaka 553, Japan **The pharmacology of 20681-S and 20682-S, 6-oxo-N-cyclopropylmethylmorphinans, as narcotic antagonist analgesics.** Archives Internationales de Pharmacodynamie et de Therapie. 241(1):79-91, 1979.

The antinociceptive and narcotic antagonistic effects of L-3-hydroxy-6-oxo-N-cyclopropylmethylmorphinan methansulfonate (20681-S) and L-3,14-dihydroxy-6-oxo-N-cyclopropylmethylmorphinan methansulfonate (20682-S) were demonstrated. Compound 20681-S exerted more potent and longer lasting antinociceptive effects than morphine or cyclazocine following oral or subcutaneous administration in rodents. The antinociceptive effect of 20682-S ranked between those of morphine and penzocine in the acetic acid writhing test in mice. Both compounds showed potent narcotic antagonistic activities; 20682-S was more active than naloxone and 20681-S was equipotent with cyclazocine. Both compounds showed fewer side-effects and less acute toxicity than reference narcotic antagonists. 11 references. (Author abstract modified)

**003209** Hlinak, Z.; Madlafousek, J. Psychiatric Research Institute, Prague, Czechoslovakia **Copulatory behaviour of castrated male rats injected with suboptimal testosterone doses.** Activitas Nervosa Superior. 21(1):52-53, 1979.

Copulatory behavior of castrated male rats injected with suboptimal testosterone doses was investigated. A critical hormonal state was identified and maintained (wherein castrated male rats received weekly testosterone doses which inhibited initiation of any copulatory behavior when exposed to a female exhibiting weak intensity of precopulatory behavior, but which allowed copulation with females performing complete precopulatory behavior). Results indicate that the transition from the precopulatory phase to the copulatory phase is delayed in the critical hormonal state, but males achieve the behavioral ejaculatory pattern in a shorter time, performing smaller number of intromissions in shorter intervals. 2 references.

**003210** Howard, K. J.; Rogers, L. J.; Boura, A. L. A. Dept. of Pharmacology, Monash University, Wellington Road, Clayton, 3168 Victoria, Australia **Functional lateralization of the chicken forebrain revealed by use of intracranial glutamate.** Brain Research. 188(2):369-382, 1980.

Injection of monosodium L-glutamate into left hemisphere of the developing chicken brain retarded visual discrimination learning and auditory habituation. Glutamate treatment of both hemispheres had the same effect, but treatment of the right hemisphere alone did not alter these behaviors. Glutamate also caused a marked increase in aggressive and sexual behavior when injected into the left hemisphere, but not when injected into both hemispheres or into the right hemisphere alone. 33 references. (Author abstract modified)

**003211** Howd, R. A.; Pryor, G. T. SRI International, Menlo Park, CA 94025 **Effect of chronic morphine on the response to and disposition of other drugs.** Pharmacology Biochemistry and Behavior. 12(4):577-586, 1980.

The effects of chronic morphine on the response to and disposition of other drugs were investigated in male Fischer rats. Ss were implanted with a total of six 75mg morphine (base) pellets over 8 days and tested on the 11th day. On day 11, a dose of 0.15mg/kg of naloxone precipitated strong withdrawal signs. Chronic treatment with morphine by this schedule inhibited weight gain but other physical effects were minimal. When tested on day 11, the morphine pelleted rats performed a pole climb conditioned avoidance response (CAR) task as well as placebo pelleted rats, either because they had become tolerant to the CAR impairing effect of the residual levels of morphine or because the residual levels of morphine were too low to affect the response. However, the impairing effects on CAR performance of pentobarbital, phenobarbital, thiopental, barbital, diazepam, and ethanol were all prolonged and/or exaggerated by the morphine pretreatment. This increase in the depressant effects of these drugs could not be completely accounted for by the effect of morphine on their uptake, distribution, or elimination. Although an interaction between the drugs and residual levels of morphine could not be ruled out, these result suggest the possibility that chronic treatment with morphine may have caused an increase in the central responsiveness to these drugs as well. 22 references. (Author abstract modified)

**003212** Hrdina, Pavel D.; von Kulmiz, Paul; Stretch, Roger. Dept. of Pharmacology, Faculty of Medicine, University of Ottawa, Ottawa, Canada **Pharmacological modification of experimental depression in infant macaques.** Psychopharmacology. 64(1):89-93, 1979.

An experimental animal model of depression, mother-infant separation in macaques, is reported, together with results of a study of pharmacological modification of this experimental depression. At the age of 6 to 8 months old, 7 macaque (M. fascicularis) infants underwent two consecutive separations from their mothers lasting 21 and 15 days, respectively. The frequency and duration of a set of individual and social behaviors were recorded throughout each of the following experimental conditions: baseline, separation, and reunion. In response to maternal separation, infants showed marked increases in frequency of behaviors reflecting distress, self-directed activity, or anxiety (e.g., vocalization, locomotion, body play). Both individual and social play behaviors were markedly suppressed in separated infants. During the second separation, one group of subjects was given, in double-blind fashion, daily doses of 5mg/kg of the antidepressant desmethylimipramine (DMI) intramuscularly. Treatment with DMI markedly diminished most of the behavioral alterations induced by separation. In particular, the increases in distress and self-directed behaviors, as well as the suppression of play activities, were prevented or antagonized. Plasma levels of DMI after 5 days of administration were in the range of 50 to 150ng/ml. 21 references. (Author abstract modified)

**003213** Hruska, Robert E.; Silbergeld, Ellen K. Bldg. 36, Rm. 4A22, NIH, Bethesda, MD 20205 **Estrogen treatment enhances dopamine receptor sensitivity in the rat striatum.** European Journal of Pharmacology. 61(4):397-400, 1980.

The effects of estrogen on striatal dopamine (DA) receptors and on behavioral response to DA agonists were studied in male Sprague-Dawley rats. Animals were injected subcutaneously with 125mcg estrogen 6 days prior to testing. Results show that the number of striatal sites labeled by 3H-spiroperidol and the intensity of apomorphine or amphetamine-induced stereotypy were significantly increased by the estrogen treatment. 10 references. (Author abstract modified)

**003214** Hulme, Miriam; Sahgal, Arjun; Iversen, Susan D. Sahgal: Dept. of Psychology, Downing Street, Cambridge CB2 3EB England **Effects of sodium amylobarbitone on memory processes in the pigeon.** Psychopharmacology. 62(1):71-78, 1979.

The effects of sodium amylobarbitone (SAB) on memory was investigated in the pigeon using a delayed pair comparison task. Performance was disrupted at all delays by 10mg/kg and 20mg/kg doses, and this effect was not due to perceptual impairment or stereotyped responding. Two other experiments assessed proactive and retroactive effects by varying the intertrial interval and by introducing an irrelevant orange stimulus at various stages of the delay interval. Although these manipulations disrupted performance, the drug did not appear to specifically potentiate their effects. The results are discussed in terms of an encoding hypothesis, and the possible neuropharmacological basis of action for SAB is considered. 38 references. (Author abstract modified)

**003215** Irving, Sharon M.; Goy, Robert W.; Davis, Gary A. 387 Tropicana Way, Union City, CA **Copulation-induced abbreviation of estrus in the female guinea pig: block by clonidine.** Pharmacology Biochemistry and Behavior. 12(5):755-759, 1980.

The alpha-adrenergic agonist clonidine blocked the inhibitory effects of coital stimulation on subsequent sexual activity in female guinea-pigs. The serotonergic antagonist methysergide and the dopaminergic antagonist pimozide had no effect. The effects of clonidine were prevented by pretreatment with the alpha-adrenergic antagonist yohimbine. Results suggest that an adrenergic system is involved in the copulation-induced inhibition of receptivity in the guinea-pig. 30 references. (Author abstract modified)

**003216** Ito, T.; Hori, M.; Yoshida, K.; Shimizu, M. Research Laboratories, Dainippon Pharmaceutical Co., Ltd., 33-94, Enoki-cho, Suita-shi, Osaka 564, Japan **Effect of anticonvulsants on experimental cortical epilepsy induced by tungstic acid gel in rats.** Archives Internationales de Pharmacodynamie et de Therapie. 241(2):287-299, 1979.

The EEG and behavioral effects of various anticonvulsants were examined in male Wistar rats made epileptic by cortical application of tungstic acid gel. Spike, spike and wave complex, and secondary generalized seizures (SGS) with high frequency components were apparent in the EEG within 1 hour of gel application. SGS often recurred with a constant interictal period over 2 to 3 hours. Head twitching, forelimb clonus, and violent convulsion with kangaroo posture were also observed. Diphenylhydantoin (10 to 40mg/kg i.v.), phenobarbital (20 and 40mg/kg), and diazepam (0.5 to 2.0mg/kg) shortened the duration of SGS and prolonged the interictal period. Trimethadione and dipropylacetate shortened the duration but did not change the interictal period. Diazepam, dipropylacetate, and taurine also suppressed interictal spikes. Results suggest that this model is suitable for predicting the effectiveness of potential anticonvulsants in epilepsies associated with the cortex. 28 references. (Author abstract modified)

**003217** Izquierdo, I.; Beamish, D. G.; Anisman, H. Departmento de Bioquimica, Instituto de Biociencias, U.F.R.G.S., 90000 Porto Alegre, RS, Brazil **Effect of an inhibitor of dopamine-beta-hydroxylase on the acquisition and retention of four different avoidance tasks in mice.** Psychopharmacology. 63(2):173-178, 1979.

The effect of [bis-(4-methyl-1-homopiperazinylthiocarbonyl)-disulfide] (FLA-63) (40 mg/kg, i.p.) on acquisition and retention in four different avoidance tasks was evaluated in mice. In all tasks animals were submitted to a training session on one day and to a retest session 24 hours later. The drug or its vehicle was given either 2 hours prior to training and retest or immedately after the training session. Two hours after injection, FLA-63 was found to lower brain norepinephrine (NE) levels by 51% without affecting those of dopamine. Pretrial administration of the drug resulted in poorer performance of step-through and step-down passive avoidance as well as of step-up active avoidance in retest sessions. The data are consistent with the hypothesis of an involvement of NE either in memory processes or in events parallel and related to memory processes. 28 references. (Author abstract modified)

**003218** Izquierdo, Ivan. Departamento de Bioquimica, Instituto de Biociencias, UFRGS (centro), 90000 Porto Alegre, RS, Brazil **Effect of naloxone and morphine on various forms of memory in the rat: possible role of endogenous opiate mechanisms in memory consolidation.** Psychopharmacology. 66(2):199-203, 1979.

The effects of naloxone and morphine on behavioral task performance and on memory channels were evaluated. Naloxone enhanced and morphine depressed retention of a standard shuttle avoidance task acquired with tone/footshock presentations. The effect of naloxone was then assessed on each of four independent memory channels known to be involved in this behavior. The channel which stores responses acquired through an avoidance mode and retrieves them in the same mode was facilitated by as little as 0.2mg/kg of the drug, while the other channels were sensitive only to 0.4 or 0.8mg/kg naloxone. Retention of a response not involving pain stimulation was also enhanced by naloxone and depressed by morphine. The results suggest a role for endogenous opiate substances as general inhibitory modulators of memory consolidation, point to a differential sensitivity of the various memory channels to naloxone (and presumably to endogenous opiate modulation), and demonstrate that the posttraining memory effects of naloxone and morphine do not depend on the presence of footshocks in the training session to become manifest. 25 references. (Author abstract modified)

**003219** Izquierdo, Juan A.; Costas, Stella Maris; Justel, Eduardo Adolfo; Rabiller, Graciela. Centro de Estudios Farmacologicos y de Principios Naturales (CEFAPRIN), CONICET, Obligado 2490, 1428 Buenos Aires, Argentina **Effect of caffeine on the memory of the mouse.** Psychopharmacology. 61(1):29-30, 1979.

The effect of caffeine on the memory of mice was examined as well as the possible relationship with the serotonin content in the brainstem, an area with serotoninergic predominance. Albino mice were injected i.p. with caffeine 10 minutes pretrial. The mice had no trial retention after 24 hours. This result suggests that caffeine, at the dose 27.9mg/kg would upset some mechanism involved in memory processes. No correlation is observed between serotonin (5-HT) increase and caffeine's effect on retention. 7 references. (Author abstract modified)

**003220** Jacobs, Carrie-Ellen. Ohio State University **The effects of dextro-amphetamine therapy versus behavioral training, alone and in combination on social behavior and responsiveness to training on hyperactive dogs. (Ph.D. dissertation).** Dissertation Abstracts International. 40(7):3472-B, 1980. Ann Arbor, Univ. Microfilms No. 8001751, 204p., 1979.

An animal model of hyperkinesis was used to determine the effects of dextro-amphetamine alone, behavioral training alone, and a combination of the two on responsiveness to training and the social behavior of 16 hyperkinetic dogs. Previous research indicated that these dogs respond to amphetamines in a manner similar to hyperkinetic children. The analyses of the data did not indicate significant overall differences between groups as a result of treatment. Reasons for the lack of significant treatment effects include small sample size, large variance on the dependent measures, and stereotypic responses on the part of eight dogs to the 0.5mg/kg dosage of dextro-amphetamine utilized. (Journal abstract modified)

**003221** Janowsky, D. S.; Abrams, A. A.; Groom, G. P.; Judd, L. L.; Cloptin, P. Department of Psychiatry, Unviersity of California, School of Medicine, La Jolla, CA 92093 **Lithium administration antagonizes cholinergic behavioral effects in rodents.** Psychopharmacology. 63(2):147-150, 1979.

The effect of lithium on cholinergic behavioral effects in rats was investigated. Physostigmine, a centrally acting cholinesterase inhibitor, antagonizes methylphenidate-induced stereotyped gnawing behavior in mice and rats. This effect is significantly attenuated when lithium chloride is concurrently administered, indicating that lithium chloride may antagonize central cholinergic activity. This observation may have theoretical implications for an adrenergic/cholinergic balance hypothesis of affective disorders. 21 references. (Author abstract)

**003222** Jeffrey, Douglas R,; Barrett, James E. Barrett: Dept. of Psychology, University of Maryland, College Park, MD 20742 **Effects of chlordiazepoxide on comparable rates of punished and unpunished responding.** Psychopharmacology. 64(1):9-11, 1979.

The effects of chlordiazepoxide (CDP) at doses of 1 to 17mg/kg on punished and unpunished responding was examined in pigeons. Identical overall rates and patterns of key pecking were maintained under a multiple fixed-interval schedule of food presentation. In one component, every 30th response produced an electric shock (punishment); whereas during the other component, the response that produced food had to be preceded by a pause of a 10 or 11 sec duration. Although CDP increased both punished and unpunished responding, greater increases were uniformly obtained with punished responding. Results are discussed with reference to previous studies. 11 references. (Author abstract modified)

**003223** Jenkins, O.; Bailey, R.; Crisp, E.; Jackson, D. M. Jackson: Dept. of Pharmacology, University of Sydney, NSW 2006, Australia **Subacute L-DOPA in mice: biochemical and behavioural effects.** Psychopharmacology. 68(1):77-83, 1980.

The locomotor stimulation induced by 200mg/kg L-DOPA and 50mg/kg benserazide (L-DOPA/B) was significantly greater in male albino mice pretreated with the same drug combination than in mice pretreated with saline. This enhanced response to L-DOPA/B was antagonized by haloperidol and pimozide. The enhanced response to L-DOPA/B challenge was also observed in mice pretreated with a high dose (1200mg/kg) of L-DOPA alone. 25 references. (Author abstract modified)

**003224** Jensen, Robert A.; Martinez, Joe L., Jr.; Vasquez, Beatriz J.; McGaugh, James L. Dept. of Psychobiology, School of Biological Sciences, University of California, Irvine, CA 92717 **Benzodiazepines alter acquisition and retention of an inhibitory avoidance response in mice.** Psychopharmacology. 64(1):125-126, 1979.

Experiments were performed to examine the effects of graded doses of diazepam, flurazepam, or lorazepam given to Swiss-Webster mice either 30 min prior to training or immediately after training in a one trial inhibitory (passive) avoidance task. A 350 micro footshock was administered following entry into a darkened compartment, and retention was tested 3 days later. Doses of 10mg/kg diazepam and 20mg/kg lorazepam given before training significantly impaired acquisition, while 1mg/kg flurazepam given immediately after training produced retrograde amnesia. These results indicate that benzodiazepines affect memory processes and that various drugs of the benzodiazepine family differentially affect acquisition and memory consolidation. 9 references. (Author abstract)

**003225** Jeste, Dilip V.; Smith, Gerard P. Smith: E. W. Bourne Behavioral Research Laboratory, New York Hospital, White Plains, NY 10605 **Unilateral mesolimbicocortical dopamine denervation decreases locomotion in the open field and after amphetamine.** Pharmacology Biochemistry and Behavior. 12(3):453-457, 1980.

The effects of unilateral mesolimbicocortical dopamine denervation on rat locomotion in the open field and after amphetamine were investigated. Unilateral denervation of the mesolimbicocortical dopaminergic (DA) system was produced by microinjections of 6-hydroxydopamine (6-OHDA) into the right or left anterolateral hypothalamus after desmethylimipramine pretreatment. Unilateral DA denervation was confirmed by the marked loss of fluorescent fibers in mesolimbic DA terminal fields in brains processed for catecholamine histofluorescence with the glyoxylic acid/paraformaldehyde method. Such unilateral DA denervation significantly decreased the locomotor exploration of an open field and the locomotor response to d-amphetamine. These results demonstrate that unilateral mesolimbicocortical DA denervation is sufficient to produce a decrease in the locomotor response to amphetamine or a decrease of locomotion in the open field. Results are consistent with the hypothesis that the mesolimbicocortical DA system energizes behavior, but does not direct it. 26 references. (Author abstract modified)

**003226** Johns, T. G.; Piper, D. C.; James, G. W. L. Piper: Roussel Laboratories Ltd., Kingfisher Drive, Swindon, Wiltshire, England **The pharmacological profile of a potential hypnotic compound RU 31158.** Archives Internationales de Pharmacodynamie et de Therapie. 240(1):53-65, 1979.

A novel benzodiazepine, 6-(orthochlorophenyl)-1,2-dihydro-2(N-methylpiperazin-1-yl)methylene-8-nitro-1H, 4H-imidazo(1,2-a)(1.4) benzodiazepin-1-one methanesulphonate (RU-31158), showed potent hynotic activity compared to diazepam in male CD-1 mice and CD rats. RU-31158 potentiated minimal hypnosis induced by hexobarbital and chlorprothixene in mice and potentiated the effects of hexobarbital in rats. Sleep studies in the rat confirmed the hypnotic properties of RU-31158 and showed that the duration of action of oral doses of 8.0 and 16.0mg/kg was not longer than 9 hours. RU-31158 also showed potent minor tranquilizer, anxiolytic, and anticonvulsant properties in a series of pharmacological tests. 22 references. (Author abstract modified)

**003227** Jolicoeur, F. B.; Wayner, M. J.; Rondeau, D. B.; Merkel, A. D. Wayner: Brain Research Laboratory, 601 University Avenue, Syracuse, NY 13210 **Effects of Phenobarbital on taste aversion induced by x-radiation.** Pharmacology Biochemistry and Behavior. 11(6):709-712, 1979.

The effects of phenobarbital on taste aversion induced by X-radiation were examined. Rats were adapted to a 23 hour 50 minutes water deprivation schedule. On the treatment day, Ss were given a novel 0.125% Na saccharin solution during the 10 minute drinking session and were then exposed to 100 rads of X-radiation. The saccharin solution was presented again on 6

subsequent test days. Phenobarbital in doses of 20, 40, 60, and 80mg/kg was administered 15 minutes prior to drinking on the first test day. Results demonstrate than phenobarbital in all doses tested has a significant attenuating effect on radiation-induced taste aversion. 12 references. (Author abstract)

**003228** Kaakkola, Seppo; Kaariainen, Ilpo. Dept. of Pharmacology, University of Helsinki, Siltavuorenpenger 10, SF-00170 Helsinki 17, Finland **Circling behavior induced by intranigral injections of GABA and muscimol in rats.** Psychopharmacology. 68(1):31-36, 1980.

Unilateral injections of GABA or muscimol into the substantia nigra of female Wistar rats produced dose dependent contralateral circling. Muscimol was much more potent that GABA and its effect lasted longer. Pretreatment with peripheral injections of bicuculline or haloperidol antagonized the circling behavior induced by intranigral GABA or muscimol. Pretreatment with atrophine increased the intensity of circling behavior induced by muscimol or GABA. Pretreatment with strychnine increased circling induced by muscimol and did not alter circling induced by GABA. Results suggest that the contralateral circling induced by intranigral injections of GABA and muscimol is dependent on the dopaminergic nigostriatal system and on the nondopaminergic nigral output system. 31 references. (Author abstract modified)

**003229** Kalivas, Peter W.; Horita, Akira. Dept. of Pharmacology, School of Medicine, University of Washington, Seattle, WA 98195 **Response to intracerebral administration of cerebrospinal fluid in the pentobarbital pretreated rat.** Neuropharmacology. 19(5):497-499, 1980.

The pH response curve for intraseptal articifical cerebrospinal fluid (CSF) was determined in male Sprague-Dawley rats. Artificial CSF was administered into the medical septal region of rats pretreated with pentobarbital. The duration of pentobarbital narcosis at pH 3.7 was significantly shorter than that in rats given CSF with pH 7.5. 8 references. (Author abstract modified)

**003230** Kaplan, Joel N. Building 18, SRI International, Menlo Park, CA 94025 **Maternal responsiveness in the squirrel monkey following chronic administration of delta9-THC.** Pharmacology Biochemistry and Behavior. 11(5):539-543, 1979.

The effects of chronic administration of THC on maternal responsiveness in the squirrel monkey were investigated. Mother squirrel monkeys were orally administered gradually increasing dosages of THC from 2 weeks to 6 months after birth, then compared with control mothers in terms of their responsiveness both to their own and to unrelated infants. In contrast to the control mothers whose response pattern clearly showed differentiation of their own and other infants, the mothers that received THC responded in much the same manner to the alien infant as they did to their own infant. The results show that the behavior of the THC exposed mothers was not attributed simply to a general reduction in their responsiveness toward their offspring or to an overall reduction in their own state of arousal. Rather, the results suggest that chronic ingestaton of delta9-THC caused the mothers to be less disturbed by separation from their infants and/or produced some degree of perceptual distortion that prevented them from responding selectively to the different infants. 17 references. (Author abstract modified)

**003231** Kaplan, Richard; Glick, Stanley D.; Goldfarb, Joseph. Goldfarb: Mount Sinai School of Medicine, CUNY, One Gustave Levy Place, New York, NY 10029 **Footshock-induced rotation: lack of effect of haloperidol and AMPT.** European Journal of Pharmacology. 61(2):179-182, 1980.

Circling behavior was induced in female Sprague-Dawley rats by footshock at 1, 2, or 4mA. The direction of circling was consistent upon retesting and was independent of the direction of spontaneous circling prior to shock. The shock-induced circling was not blocked by haloperidol or alpha-methyl-p-tyrosine. Results indicate that the circling induced by aversive stimuli is not mediated by the nigrostriatal dopamine system. 8 references. (author abstract modified)

**003232** Kastin, Abba J.; Jemison, Michael T.; Coy, David H. Veterans Administration Medical Center, New Orleans, LA 70146 **Analgesia after peripheral administration of enkephalin and endorphin analogues.** Pharmacology Biochemistry and Behavior. 11(6):713-716, 1979.

Several analogues of Met-enkephalin and beta-endorphin were tested for their analgesic properties after systemic injection. The latencies of mice to flick their tails away from a source of heat revealed that analogues of the opiate peptides can cause analgesia when injected by this route. In particular, compounds specifically designed to be more lipophilic or to possess additional binding sites were shown to be potent analgesic agents after peripheral administration. 12 references. (Author abstract)

**003233** Kastin, Abba J.; Olson, Richard D.; Ehrensing, Rudolph H.; Berzas, Matthew C.; Schally, Andrew V.; Coy, David H. Veterans Administration Medical Center, New Orleans, LA 70146 **MIF-I's differential actions as an opiate antagonist.** Pharmacology Biochemistry and Behavior. 11(6):721-723, 1979.

The effects of MIF-I (Pro-Leu-Gly-NH2) were examined in three experimental conditions in which the opiate antagonist naloxone was active. MIF-I was found to block the analgesic effect of enkephalins and also morphine in the tail flick test but not in the vas deferens assay. Unlike naloxone, MIF-I did not seem to reduce food intake in ventromedial hypothalamus lesioned rats. Results suggest the possibility that MIF-I may represent a class of naturally occurring opiate antagonists with varying activities in independent situations. 11 references. (Author abstract)

**003234** Katz, Jonathan L.; Barrett, James E. Harvard Medical School, Dept. of Psychiatry, 25 Shattuck Street, Boston, MA 02115 **Effects of d-amphetamine and ethanol alone and in combination on schedule-controlled responding in pigeons.** Psychopharmacology. 64(1):13-18, 1979.

The effects of d-amphetamine and ethanol, alone or in combination, were examined in 5-min fixed interval (FI) or 30 response fix-ratio (FR) schedules of food delivery in pigeons. d-Amphetamine (.1 to 1mg/kg) either increased or did not affect overall rates of responding under FI; the lowest dose of ethanol (.5g/kg) did not affect or slightly decreased response rates, whereas higher doses (1 to 2mg/kg) substantially decreased rates. Combinations of low noneffective ethanol doses with most doses of d-amphetamine increased rates of responding under FI above those obtained with d-amphetamine alone; decreases produced by higher ethanol doses were attenuated by most doses of d-amphetamine. Doses of d-amphetamine (.1 to 1mg/kg) and ethanol (.5 to 1.5g/kg) alone generally had no effect on FR responding; higher doses of these drugs decreased responding. The effects of dose combinations other than the highest ones generally differed little from those obtained with ethanol alone; the effects of high doses of each drug were antagonized by low to moderate doses of the other. Combinations of ethanol and d-amphetamine can result in higher rates of responding than are obtained with either alone. Further, drug effects, alone or in combination, depend on the schedule under which the behavior is maintained. 20 references. (Author abstract modified)

**003235** Katz, R. J. Mental Health Research Institute, Dept. of Psychiatry, University of Michigan Medical Center, Ann Arbor, MI 48109 **Inhibition-mediating dopamine receptors and the control of intracranial reward.** Psychopharmacology. 61(1):39-41, 1979.

The effects of an inhibition mediating (IM) receptor agonist and antagonist upon responding for rewarding brain stimulation was examined in 12 adult male rats. A receptor selective agonist and antagonist of IM dopamine receptors (type II receptors) produced significant and dose related alterations in bar-pressing for intracranial reward. Receptor inhibition by piribedil increased responding for reward while receptor activation by 3,4-dihydroxyphenylamino-2-imidazoline reduced responding. IM receptors may therefore play a role opposite to classic excitation mediating receptors in controlling reward. 17 references. (Author abstract modified)

**003236** Katz, R. J.; Carroll, Bernard J. Mental Health Research Institute, University of Michigan, 205 Washtenaw Place, Ann Arbor, MI 48109 **Enkephalin-dopamine interactions in behavioral arousal.** Progress in Neuro-Psychopharmacology. 3(4):395-398, 1979.

Central injection of a long-lasting enkephalin analog D-Ala2-leu-enkephalinamide, produced a stereotyped motor activity in male Swiss-Webster mice. This activation syndrome was significantly reduced by the dopamine (DA) receptor blockers pimozide and fluspririlene and by (3,4-dihydroxyphenylamino)-2-imidazoline, an agonist of inhibitory DA receptors. Results suggest that the behavioral effects of enkephalins are dependent at least in part upon intact DA systems and that enkephalin and DA systems share a close functional relationship. 11 references. (Author abstract modified)

**003237** Katz, R. J.; Schmaltz, Kristine. Mental Health Research Institute, Dept. of Psychiatry, University of Michigan Medical Center, Ann Arbor, MI 48109 **Facilitation of opiate- and enkephalin-induced motor activity in the mouse by phenytoin sodium and carbamazepine.** Psychopharmacology. 65(1):65-68, 1979.

The effect of drug pretreatment upon morphine-induced motor activity in grouped mice was examined. Compared to the influence of vehicle, the motor activity of morphine injected mice was increased. Neither phenytoin sodium nor carbamazepine alone facilitated motor activity, but pretreatment with both drugs further facilitated the increased motor activity produced by morphine. In a second experiment, mice were injected centrally with a long-acting analog of leu-enkephalin. It also increased motor activity in comparison with vehicle. Again, both phenytoin sodium and carbamazepine further facilitated this response. Both experiments suggest a facilitatory interaction between some aspects of these anticonvulsants and opiate induced motor activity. 18 references. (Author abstract modified)

**003238** Kellogg, Carol; Tervo, Donna; Ison, James; Parisi, Thomas; Miller, Richard K. Dept. of Psychology, University of Rochester, Rochester, NY **Prenatal exposure to diazepam alters behavioral development in rats.** Science. 207(4427):205-207, 1980.

Behavioral activity and reactivity were studied in developing rats exposed to diazepam during the last week of gestation. Characteristic potentiation of rat locomotion responses and acoustic startle reflexes that normally appear in the third postnatal week was absent in the diazepam exposed rats. Loss of these behaviors suggests a long-term effect that may result from changes in cellular development. Tissue undergoing neuronal differentiation may be especially sensitive to drugs that act on the central nervous system, and the period in which differentiation occurs is perhaps critical for the induction of changes that are later expressed as altered behavior. 34 references. (Author abstract modified)

**003239** Kelly, Joe; Grossman, Sebastian P. Dept. of Anatomy and Neurobiology, Washington University School of Medicine, 660 South Euclid Avenue, St. Louis, MO 63110 **GABA and hypothalamic feeding systems. II. A comparison of GABA, glycine and acetylcholine agonists and their antagonists.** Pharmacology Biochemistry and Behavior. 11(6):647-652, 1979.

The effects on feeding behavior of microinjections of GABA, glycine, and acetylcholine agonists and their antagonists into the paraventricular hypothalamic nucleus (PVH) were investigated. During the light phase of the lighting cycle, injections of 0.3mcl of muscimol (100ng) and flurazepam diHCl (20mcg) increased feeding. Similar injections of glycine (500ng) did not influence feeding during the light phase. During the dark phase, 0.3mcl injections of bicuculline methiodide (30ng) and picrotoxin (160ng) suppressed feeding. Similar injections of carbachol increased drinking during the dark phase. Injections of strychnine during this phase were without effect. Tilt box activity levels were not altered by injection of picrotoxin (160ng) into the PVH. 32 references. (Author abstract modified)

**003240** Kiianmaa, Kalervo. Research Laboratories of the State Alcohol Monopoly (Alko), Box 350, SF-00101 Helsinki 10, Finland **Alcohol intake and ethanol intoxication in the rat: effect of a 6-OHDA-induced lesion of the ascending noradrenaline pathways.** European Journal of Pharmacology. 64(1):9-19 1980.

The role of central noradrenergic neurons in the control of ethanol intake and expression of ethanol intoxication were demonstrated in male Long-Evans rats. Three weeks after bilateral injection of 6-hydroxydopamine (6-OHDA) into the posterior mesencephalon, a transient increase in ethanol intake was observed. The performance of the 6-OHDA treated rats in the tilting plane test more impaired than that of control rats by ethanol (2g/kg i.p.), but the hypothermic effect of ethanol (4g/kg i.p.) was significantly smaller in the 6-OHDA treated rats. Catecholamine levels in various parts of the brain could be correlated with the extent of ethanol intoxication and hypothermia. The duration of ethanol-induced narcosis was not affected by 6-OHDA. 41 references. (Author abstract modified)

**003241** Kilbey, M. Marlyne; Ellinwood, Everett H., Jr. Behavioral Neuropharmacology Section, Department of Psychiatry, Duke University Medical Center, P.O. Box 3870, Durham, NC 27710 **Discriminative stimulus properties of psychomotor stimulants in the cat.** Psychopharmacology. 63(2):151-153, 1979.

The discriminative stimulus properties of psychomotor stimulants were investigated in cats. Cats were trained to choose between two levers of an operant chamber using interoceptive cues provided by d-amphetamine or saline as the discriminative stimuli. Following training, stimulus generalization was observed to additional doses of d-amphetamine and cocaine, but not to morphine. Clozapine blocked the generalization of the drug discrimination response to d-amphetamine, but had no effect on generalization to cocaine. These data indicate that discriminative stimulus properties of psychomotor stimulants, previously described in rats, are similar in cats. 9 references. (Author abstract)

**003242** King, Bruce M.; Castellanos, F. Xavier; Kastin, Abba J.; Berzas, Matthew C.; Mauk, Michael D.; Olson, Gayle A.; Olson, Richard D. Dept. of Psychology, University of New Orleans, New Orleans, LA 70122 **Naloxone-induced suppression of food intake in normal and hypothalamic obese rats.** Pharmacology Biochemistry and Behavior. 11(6):729-732, 1979

Intraperitoneal injections of naloxone hydrochloride (1, 2, 4, and 8mg/kg) suppressed food intake in both normal and hypothalamic obese rats maintained on a 4 hour per day feeding schedule. The decrease in feeding was more pronounced in the animals with ventromedial hypothalamic lesions. Appetitively motivated feeding, i.e., the consumption of sweetened milk under nondeprived conditions, was also suppressed by naloxone, but there was no reliable difference between groups. It is concluded that opiate receptors located in the ventromedial hypothalamus are not essential for the effects of opiate agonists and antagonists on feeding behavior. 21 references. (Author abstract modified)

**003243** King, Maurice G.; Kastin, Abba J.; Olson, Richard D.; Coy, David H. Dept. of Psychology, University of Newcastle, N.S.W., 2308, Australia **Systemic administration of met-enkephalin, (D-Ala2)-met-enkephalin, beta-endorphin, and (D-Ala2)-beta endorphin: effects on eating, drinking and activity measures in rats.** Pharmacology Biochemistry and Behavior. 11(4):407-411, 1979.

Activity and food and water intake were measured in male rats given four daily injections (80mcg/kg i.p.) of met-enkephalin, (D-Ala2)-met-enkephalinamide, beta-endorphin, (D-Ala2)-beta-endorphin, or vehicle. Met-enkephalin had no effects in these tests, but its D-Ala2 analog reduced food intake and had complex effects on activity. Beta-endorphin did not affect food or water intake, but did alter activity; animals treated with beta-endorphin were less active in familiar situations and more active in novel situations than controls. Wheel running activity over a 24 hour period was reduced by (D-Ala2)-beta endorphin. 10 references. (Author abstract modified)

**003244** Kirby, M. L. Dept. of Anatomy, Medical College of Georgia, Augusta, GA 30912 **Effects of morphine on spontaneous activity of 18-day rat fetus.** Developmental Neuroscience. 2(5):238-244, 1979.

The effects of morphine on spontaneous activity of 18-day-old fetal rats were examined in utero. Morphine injected subcutaneously in the dam caused a decrease in fetal spontaneous activity which was dose dependent. Activity returned to control levels following naloxone administration to the dam. Fetuses which had been chronically exposed to morphine from days 7 through 17 and observed on day 18 of gestation became hyperactive following administration of naloxone to the dam. It is suggested that this may represent fetal withdrawal. 20 references. (Author abstract modified)

**003245** Kitahama, Kunio; Valatx, Jean-Louis. Department de Medecine experimentale, Universite Claude-Bernard, 8 avenue Rockefeller, F-69373 Lyon Cedex 2, France **Strain differences in amphetamine sensitivity in mice. I. A diallel analysis of open field activity.** Psychopharmacology. 66(2):189-194, 1979.

Differences in amphetamine sensitivity and open-field activity were studied in pigmented and albino strains of mice. Previous experiments have reported that 1mg/kg d-methylamphetamine HCl induced hyperactivity in pigmented strains (C57BR, C57BL/6, and SEC) and hypoactivity or no change in albino strains (BALB/c, A, and AKR) of mice. In F1 hybrids, the B6 genotype was partially dominant over BR and C, and BR over C. In animals back crossed to C parents widespread distributions with two peaks were obtained in control experiments, and amphetamine-induced hyperactivity in 38% of the albino population, and hypoactivity or no significant change in 45% of the pigmented one. Results indicate that genes influencing locomotor activity are independent from those influencing amphetamine sensitivity. From results obtained in back crosses and C57BL/6-c2J mice, the albino gene does not seem to be involved in the hypoactive effect of amphetamine, although some genes located on the same chromosome may be involved. 27 references. (Author abstract modified)

**003246** Knoll-Kohler, E.; Wojnorowicz, F.; Sarkander, H.-J. Pharmakologisches Institut, Freie Universitat Berlin, Thielallee 69/73, D-1000 Berlin 33, Germany **Correlated changes in neuronal cerebral rat brain RNA synthesis and hypo- and hypermotoric disorders induced by 6-aminonicotinamide (6-AN).** Experimental Brain Research. 38(2):173-179, 1980.

Neuronal and nonastrocytic glial cerebral and cerebellar in vitro RNA synthesis was determined in Wistar rats during the hypomotoric and hypermotoric stages induced in vivo by administration of the nicotinamide antagonist 6-aminonicotinamide on postnatal day 7. Significant changes in the rate of neuronal cerebral and cerebellar RNA synthesis coinciding with the different phases of motor activity were observed. However, only the changes in neuronal cerebral RNA synthesis were directly proportional to the changing pattern of motor activity. (Author abstract modified)

**003247** Kokkinidis, Larry; Anisman, Hymie. Dept. of Psychology, University of Saskatchewan, Sakatoon, Saskatchewan, Canada **Circling behavior following systematic d-amphetamine administration: potential noradrenergic and dopaminergic involvement.** Psychopharmacology. 64(1):45-54, 1979.

Four experiments were conducted to further elucidate factors in d-amphetamine-induced rotational behavior in mice. Systemic treatment with d-amphetamine produced a dose dependent increase in the circling behavior of normal mice. Treatment with both alpha-methyltyrosine (alpha-MpT) and FLA-63 antagonized the amphetamine-induced circling behavior. Similarly, blockade of beta-adrenergic receptors by propranolol and dopamine receptors by haloperidol reversed the circling response elicited by amphetamine. In contrast to alpha-MpT and haloperidol, however, neither FLA 63 nor propranolol attenuated the locomotor excitation engendered by amphetamine. Following repeated d-amphetamine injection, the circling ordinarily induced by a single injection was abolished, whereas the locomotor effects of amphetamine remained unaltered. These findings are consistent with earlier work suggesting that tolerance may occur in those behaviors that involve a noradrenergic component. Possible mechanisms of this tolerance to amphetamine-induced perseveration are discussed. 29 references. (Author abstract modified)

**003248** Kokkinidis, Larry; Zacharko, Robert M. University of Saskatchewan, Saskatoon, Saskatchewan, Canada S7N OWO **Enhanced self-stimulation responding from the substantia nigra after chronic amphetamine treatment: a role for conditioning factors.** Pharmacology Biochemistry and Behavior. 12(4):543-547, 1980.

Rats treated with 2mg/kg of d-amphetamine and tested for self-stimulation responding supported from the substantia nigra (pretrial group), showed a progressive augmentation in rates of self-stimulation responding relative to control animals following repeated drug/test pairings for 10 days. A similar behavioral profile was not observed among animals that received behavioral testing followed by drug administration (posttrial group) during the chronic phase. On test day (day 11), rats that received repeated drug/test pairings during the chronic phase exhibited a facilitated self-stimulation response to a low test dosage of d-amphetamine which otherwise had no behavioral effect, whereas rats exposed to chronic test/drug pairings during the chronic phase did not show enhanced self-stimulation rats to the test dosage of d-amphetamine. Animals chronically treated with pretrial injections of amphetamine also showed fa-

cilitated self-stimulation responding when tested with saline, relative to animals that were chronically treated with posttrial injections of amphetamine and tested with saline. These findings were not parallelled by drug-induced changes in locomotor activity. Response sensitivation after chronic amphetamine treatment does not appear to involve the accumulation to the drug in adipose tissue. A role for conditioning factors in the development of the response sensitization is discussed. 15 references. (Author abstract)

**003249** Kokkinidis, Larry; Zacharko, Robert M. Dept. of Psychology, University of Saskatchewan, Saskatoon, Saskatchewan, Canada S7N OWO **Response sensitization and depression following long-term amphetamine treatment in a self-stimulation paradigm.** Psychopharmacology. 68(1):73-76, 1980.

The effects of long-term amphetamine treatment on responding supported by self-stimulation of the substantia nigra were evaluated. Male CD rats repeatedly treated with d-amphetamine and then tested with a low dose of the drug that ordinarily has no behavioral effects showed higher response rates than animals injected repeatedly with saline and tested with the same low dose of amphetamine. Responding was depressed in animals given long-term treatment with amphetamine and tested with saline. Results are discussed in relation to animal models of amphetamine psychosis and postamphetamine depression in humans. 20 references. (Author abstract modified)

**003250** Kokkinidis, Larry; Zacharko, Robert M. Dept. of Psychology, University of Saskatchewan, Saskatoon, Saskatchewan, S7N OWO, Canada **Intracranial self-stimulation in mice using a modified hole-board task: effects of d-amphetamine.** Psychopharmacology. 68(2):169-171, 1980.

Male Swiss mice (n=18) implanted with stimulating electrodes in the lateral hypothalamus demonstrated reliable self-stimulation rates when given the opportunity to break a photobeam in a modified hole board task. Self-stimulation rates were enhanced by low doses of d-amphetamine and depressed by high doses. A possible interaction between the rewarding properties of electrical brain stimulation and the reinforcing properties of amphetamine is discussed. 7 references. (Author abstract modified)

**003251** Kraemer, Gary W.; Klopf, Fredric H.; McKinney, William T. Psychology Dept. Primate Laboratory, University of Wisconsin, 22 N. Charter Street, Madison, WI 53706 **Mutual antagonism of behavioral effects of TRH and thiobarbiturate on an operant task in rhesus monkeys.** Psychopharmacology. 61(1):103-104, 1979.

Similar excitatory or depressant response rate dependent effects on monkeys responding on a variable-interval reinforcement schedule were observed following intravenous administration of either thyrotropin releasing hormone (TRH) or thiobarbiturate. However, these agents were mutually antagonistic when given together even though the response rate altering effects of each agent were in the same direction. These findings establish an additional behavioral effect of exogenously administered TRH in primates and suggest that barbiturates might alter behavior in part through an interaction with brain TRH receptive mechanisms. 4 references. (Author abstract)

**003252** Kulkosky, Paul J. Edward W. Bourne Behavioral Research Laboratory, New York Hospital-Cornell Medical Center, 21 Bloomingdale Road, White Plains, NY 10605 **Reduction of drinking-associated feeding by C-terminaloctapeptide of cholecystokinin-pancreozymin.** Behavioral and Neural Biology. 29(1):111-116, 1980.

Water deprived Wistar rats were presented with a novel almond extract solution 15 minutes after i.p. injections of the C-terminal octapeptide of cholecystokinin-pancreozymin or lithium chloride. The octapeptide significantly reduced drinking associated feeding, but not fluid intake. Both fluid and food intakes were suppressed in the lithium treated group. Conditioned taste aversion to the novel solution was evident only in the lithium group in a subsequent two bottle test. 12 references. (Author abstract modified)

**003253** Kuribara, Hisashi; Tadokoro, Sakutaro. Div. for Behavioral Analysis, Behavior Research Institute, School of Medicine, Gunma University, 3-39-22 Showa-machi, Maebashi 371, Japan **Effects of fluphenazine enanthate and fluphenazine decanoate on discriminated avoidance response and water drinking behavior in rats.** Psychopharmacology. 65(1):1-6, 1979.

Effects of the long acting neuroleptic drugs fluphenazine enanthate (FE) and flurphenazine decanoate (FD) on discriminated avoidance response and daily patterns of water drinking behavior in rats were studied. It was found that both FE and FD exert specific strong and prolonged inhibitory effects on the conditioned avoidance response without making substantial changes on fundamental behaviors such as eating and drinking. The present finding is considered to have an important significance in the preclinical evaluation of the drugs. 22 references. (Author abstract modified)

**003254** Kutscher, Charles L.; Yamamoto, Bryan K. Psychology Research Laboratory, Syracuse University, Syracuse, NY 13210 **A frequency analysis of behavior components of the serotonin syndrome produced by p-chloroamphetamine.** Pharmacology Biochemistry and Behavior. 11(6):611-616, 1979.

A time sampling frequency analysis of behavioral components of the serotonin syndrome observed following injection of 2.5 to 10mg/kg dosages of p-chloroamphetamine (PCA) is described. Stereotypic behavior of rats (forepaw treading, circling, head weaving and inching) increased with increasing dosages and normal behaviors (grooming, rearing, and instances of inactivity) decreased. Composite scores of stereotypic behavior were a positive, linear function of PCA dosage. Composite scores of normal behavior showed near maximal inhibition at 5mg/kg. Splayed hindlimbs is a reliable and sensitive indicator of PCA action, but vocalization, tremors, diarrhea, and autonomic signs are not. Preinjection of PCA strongly attenuated the PCA-induced syndrome, as expected, since the preinjection should deplete brain serotonin and reduce the amount released by the second PCA injection. 14 references. (Author abstract modified)

**003255** Larson, Alice A.; Vaught, Jeffrey L.; Takemori, A. E. Dept. of Veterinary Biology, University of Minnesota, St. Paul, MN **The potentiation of spinal analgesia by leucine enkephalin.** European Journal of Pharmacology. 61(4):381-383, 1980.

Intrathecal administration of morphine and met-enkephalin produced dose dependent analgesia in Sprague-Dawley and Long-Evans hooded rats in the tail flick assay. Pretreatment with leu-enkephalin at a dose that had no analgesic effect significantly reduced the median effective doses of both morphine and met-enkephalin. Pretreatment with met-enkephalin at similar subanalgesic doses had no effect. 10 references. (Author abstract modified)

**003256** Lassen, J. Buus. Dept. of Pharmacology, A/S Ferrosan, Research Division, Sydmarken 5, DK-2860 Soborg, Denmark **Inhibition of apomorphine-induced climbing in mice by cholinergic drugs and neuroleptics.** Acta Pharmacologica et Toxicologica. 45(2):161-165, 1979.

Subcutaneous administration of 1mg/kg apomorphine to female NMRI mice housed in individual cages elicited abnormal vertical climbing behavior. This effect was inhibited by physostigmine, oxotremorine, clozapine, or haloperidol. A small, inactive dose of physostigmine potentiated the effect of clozapine, but not that of haloperidol. Atropine antagonized the effect of physostigmine, oxotremorine, clozapine, and haloperidol. Results suggest that the climbing behavior induced by dopamine receptor stimulation can be antagonized by blockage of dopamine receptors or by activation of muscarinic receptors. The possibility that a muscarinic effect may contribute to the antipsychotic action of clozapine is considered. 44 references. (Author abstract modified)

**003257** Laychock, S. G.; Johnson, D. N.; Harris, L. S. Dept. of Pharmacology, Medical College of Virginia, Richmond, VA 23298 **PGD2 effects on rodent behavior and EEG patterns in cats.** Pharmacology Biochemistry and Behavior. 12(5):747-754, 1980.

Prostaglandin-D2 (PGD2, 0.45 to 4.05mg/kg i.v.) decreased spontaneous locomotor activity in Sprague-Dawley rats, but did not impair the neuromuscular coordination of mice treated with the same doses. PGD2 increased pentobarbital sleeping time in mice in a dose dependent fashion, but did not prevent convulsions induced by electrochock or pentylenetetrazol. In cats, the characteristic response to PGD2 infusion (16 to 3000mcg) was the conversion from a uniform low voltage, fast wave EEG pattern to high voltage, slow waves; the cats were sedated and sometimes catatonic and showed brief period of hypotension, bradycardia, diarrhea, analgesia, and hyperthermia at high doses. 25 references. (Author abstract modified)

**003258** Lazareno, S. Dept. of Psychology, University of Reading, Whiteknights, Reading, England **d-Amphetamine and punished responding: the role of catecholamines and anorexia.** Psychopharmacology. 66(2):133-142, 1979.

The selective suppressant effect of d-amphetamine on responding in stress situations was investigated. Rats were trained to press a lever for food on a schedule in which components of variable interval reinforcement alternated with conflict components in which every response resulted in food delivery and footshock. Low doses of d-amphetamine selectively suppressed responding in the conflict component in a dose dependent manner, whereas prefeeding suppressed responding in both components. Pretreatment with noradrenergic blocking agents did not diminish the suppressant effect of d-amphetamine, but this effect was reduced by pretreatment with alpha-methyl-para-tyrosine methylester and dopamine blockers indicating that d-amphetamine was exerting its selective suppressant effect via the release of dopamine. It is suggested that the effects of low doses of d-amphetamine on behavior in conflict situations may provide a useful model for investigating the mode of action of neuroleptic drugs. 55 references. (Author abstract modified)

**003259** Le Magnen, J.; Marfaing-Jallat, P.; Miceli, D.; Devos, M. Lab de Neurophysiologie Sensorielle et Comportementale, College de France, 11, Place Marcelin Berthelot, F-75231 Paris Cedex 05, France **Pain modulating and reward systems: a single brain mechanism?** Pharmacology Biochemistry and Behavior. 12(5):729-733, 1980.

Naloxone (1mg/kg) enhanced the spontaneous aversion to quinine hydrochloride and a conditioned aversion to a saccharin solution in male Wistar rats. The drug also acutely abolished the preference for sweet solutions versus water. It is suggested that brain rewarding and pain modulating systems involve a common, naloxone blockable opiate system. 47 references. (Author abstract modified)

**003260** Leander, J. David. Dept. of Pharmacology, School of Medicine, 231H, University of North Carolina, Chapel Hill, NC 27514 **Comparison of morphine, meperidine, anileridine, and alphaprodine on schedule-controlled responding and analgesia.** Pharmacology Biochemistry and Behavior. 12(5):797-801, 1980.

Morphine, meperidine, alphaprodine, and anileridine decreased rates of lever-pressing under a fixed-ratio 20 response schedule of food presentation and increased latencies for tail withdrawal from warm water in male Sprague-Dawley and Long-Evans rats. Naloxone antagonized the effects of all four narcotics on tail withdrawal. The narcotic antagonist also shifted the dose/effect curves for morphine, alphaprodine, and anileridine for lever-pressing, but did not antagonize the rate decreasing effect of meperidine. Results suggest that the analgesic effect of meperdine is mediated by a narcotic action, while the drug's effect on schedule controlled responding is mediated by a different mechanism. 21 references. (Author abstract modified)

**003261** Leccese, Arthur P.; Grant, Douglas S. Grant: Dept. of Psychology, University of Alberta, Edmonton, Alberta T6G 2E9, Canada **Posttrial injections of strychnine sulfate: facilitation of consolidation or retrieval?** Animal Learning & Behavior. 8(2):258-264, 1980.

Animals given strychnine sulfate shortly after training and displaying enhanced retention 24 hours later were examined to determine if the process is due to facilitation of consolidation or retrieval. A test with Sprague-Dawley rats failed to support the consolidation interpretation, but did support the retrieval interpretation. It is concluded that a retrieval model provides an adequate interpretation of the facilitation of retention resulting from posttrial injections of strychnine, and that an unambiguous demonstration that strychnine enhances processes of consolidation has yet to be offered. 29 references. (Author abstract modified)

**003262** Leshner, Alan I.; Remler, Helga; Biegon, Anat; Samuel, David. Dept. of Psychology, Bucknell University, Lewisburg, PA 17837 **Desmethylimipramine (DMI) counteracts learned helplessness in rats.** Psychopharmacology. 66(2):207-208, 1979.

The hypothesis was tested that prior exposure to inescapable aversive stimuli produces decreases in central catecholamine levels which, in turn, interfere with later adaptive responding. Rats were exposed to either inescapable preshocks or control procedures, treated with one of three doses of DMI, and tested for later adaptive responding. DMI, a catecholamine modulator, attenuated the deficits in escape responding that ordinarily follow prior exposure to inescapable preshocks, and it did so in a dose dependent fashion. These findings support the position that the learned helplessness phenomenon is mediated by catecholamine changes. 6 references. (Author abstract modiifed)

**003263** Lesse, Henry; Collins, Jeremiah P. Dept. of Psychiatry and Biobehavioral Sciences, School of Medicine, University of California, Los Angeles, Los Angeles, CA 90024 **Effects of cocaine on propagation of limbic seizure activity.** Pharmacology Biochemistry and Behavior. 11(6):689-694, 1979.

The effects of cocaine on the spread of epileptiform discharges within the limbic system were studied in cats prepared with bilateral arrays of indwelling electrodes. Low frequency focal electrical stimulation at threshold intensity was employed to initiate after discharges in the hippocampus and amygdala. Latencies for the propagation of epileptiform activity to distant limbic sites were determined. Saline and drug tests were alternated, with 96 hours intervals between cocaine administrations. Three subconvulsant doses (1 to 10mg/kg cocaine hydrochloride, injected intramuscularly) were tested in a counterbalanced order. Cocaine administration significantly increased the speed at which epileptiform discharges spread to the amygdala and to

the hippocampus. This effect was dose related, it followed both hippocampal and amygdala stimulation and was evident in ipsilateral as well as contralateral projection sites. These changes were found when limbic seizure patterns were localized and also after fully developed motor convulsions were evoked. In addition, cocaine decreased the duration of the propagated discharges. These results suggest that subconvulsive doses of cocaine have an excitatory effect on the hippocampus and amygdala, increasing their sensitivity to repetitive discharges originating in distant sites. A concurrent inhibitory effect is suggested by the decreased duration of the propagated discharges. 33 references. (Author abstract)

**003264** Liebman, Jeffrey M.; Pastor, Gary. Research Dept., Pharmaceuticals Division, Ciba-Geigy Corp., Summit, NJ 07901 **Antinociceptive effects of baclofen and muscimol upon intraventricular administration.** European Journal of Pharmacology. 61(3):225-230, 1980.

Intraventricularly administered baclofen (1mcg) and muscimol (0.1mcg) greatly reduced vocalization and motor responses to nociceptive pinch in male Wistar rats, but did not alter tail flick responding. Systemic administration of baclofen resulted in markedly attenuated of both tail flick and pinch responding, whereas systemic administration of muscimol produced only weak antinociception. Muscle relaxation was less apparent after intraventricular administration of muscimol than after baclofen. Results suggest that baclofen's antinociceptive action may be mediated by a supraspinal GABA substrate, as well as by a spinal component that may not directly involve GABA. 24 references. (Author abstract modified)

**003265** Livingstone, Margaret S.; Harris-Warrick, Ronald M.; Kravitz, Edward A. Dept. of Neurobiology, Harvard Medical School, Boston, MA 02115 **Serotonin and octopamine produce opposite postures in lobsters.** Science. 208(4439):76-79, 1980

The behavioral effects of serotonin and octopamine on lobsters and crayfish were studied. Injected into the circulation of freely moving lobsters and crayfish, octopamine produced sustained extension of the limbs and abdomen while serotonin produced sustained flexion. Neurophysiological analyses show that these postures can be accounted for by opposing, coordinated effects of these amines on patterns of motoneuron activity recorded from the ventral nerve cord. Other possible mechanisms are discussed, as are analogous paired amine effects on motoneuron activity of other organisms. 16 references. (Author abstract modified)

**003266** Louie, Alan K. Laboratory of Psychobiology, Harvard Medical School, 25 Shattuck St., Boston, MA 02115 **Effects of d-amphetamine and pentobarbital under concurrent fixed-ratio schedules.** Journal of the Experimental Analysis of Behavior. 34(1):107-116, 1980.

The effects of d-amphetamine and pentobarbital on key peck responding by pigeons were examined with a fixed-ratio schedule. Doses of d-amphetamine decreased rates on both minor and major keys and slightly increased the asymmetric distribution of responses, while pentobarbital reversed the distribution of responses by increasing low rates and decreasing high rates. The pigeons maintained their original asymmetric distribution of responses during the 1.5 year long study, despite schedule alterations and drug administrations. The differential effects of d-amphetamine and pentobarbital on responding may reflect the effects of these drugs on suppressed responding. 18 references. (Author abstract modified)

**003267** Loullis, Costas C.; Wayner, Matthew J. Wayner: Brain Research Laboratory, Syracuse University, 601 University Avenue, Syracuse, NY 13210 **Effects of imipramine on schedule dependent and schedule induced behavior.** Pharmacology Biochemistry and Behavior. 11(6):725-728, 1979.

The effects of imipramine on schedule-dependent and schedule-induced behavior were investigated. Rats were reduced to 80% bodyweight and were exposed to a fixed-interval 1 minute reinforcement schedule for 60 minutes daily until lever presses, licks, and water consumption stabilized for at least 10 days. In Experiment 1, animals were injected with 0.9% saline, 2, 4, 8, and 16mg/kg of imipramine in a counterbalanced design. In Experiment 2, following the return of all three measures to preinjection baseline, the same animals were injected with 16mg/kg of imipramine daily for 8 days. On days 9 through 11, animals continued to be tested under the same conditions but imipramine was not administered. Results of Experiment 1 reveal a significant decrease in lever presses at 8mg/kg and a decrease in lever presses and water intake at 16mg/kg. Licks were not significantly different from saline baseline at any of the doses used. In Experiment 2, repeated administration of imipramine resulted in a significant decrease in lever presses from saline baseline on all days. Water intake was significantly depressed on day 2 through 8. Licks were depressed on days 2, 3, 4, 5, and 8. Animals did not show any tolerance to the repeated administration of the drug. Licks and water consumption were not significantly different from saline baseline on days 9, 10, and 11. Lever presses returned to baseline on day 10. These data indicate that imipramine produces differential and dose dependent effects on schedule-dependent and schedule-induced behavior. 15 references. (Author abstract modified)

**003268** Lowy, Martin T.; Maickel, Roger P.; Yim, George K. W. Dept. of Pharmacology & Toxicology, School of Pharmacy & Pharmacal Sciences, Purdue University, West Lafayette, IN 47907 **Naloxone reduction of stress-related feeding.** Life Sciences. 26(24):2113-2118, 1980.

The effects of the narcotic antagonist, naloxone, on various types of stress related feeding in rats were examined. Tail pinch induced eating of a palatable substance, and 3 hour daytime rat chow intake following acute 2-deoxy-D-glucose (2-DG) administration or 24 hour food deprivation were significantly decreased by low doses of naloxone. Nighttime food intake was likewise decreased by naloxone. In contrast, hyperphagia induced by insulin was not decreased by naloxone. These findings suggest that narcotic antagonists should be considered as possible anorexics selective for stress-induced eating and that endogenous opiates may prove to be another significant factor involved in the control of food intake. 25 references. (Author abstract)

**003269** Lucas, E. A.; Rogers, J.; Sterman, M. B. Dept. of Anatomy, University of Arkansas for Medical Sciences, Little Rock, AR 72201 **Effect of amphetamine and pentobarbital on sleep-wake patterns of cats with basal forebrain lesions.** Psychopharmacology. 68(2):179-184, 1980.

The effects of amphetamine and pentobarbital were studied in cats with basal forebrain lesions that induce insomnia. Amphetamine increased alertness and decreased slow wave sleep (SWS) and REM sleep for up to 12 hours in intact or lesioned cats. Pentobarbital inhibited REM sleep and alert states and increased SWS and drowsy states in intact animals; similar effects were seen in lesioned cats, except the amount of REM sleep was significantly elevated. Results suggest that pentobarbital mimics the normal inhibitory influence of the intact forebrain and induces or facilitates normal sleep patterns in cats with forebrain lesions. 40 references. (Author abstract modified)

**003270** Lucki, Irwin. University of Iowa **Response rate and rate of reinforcement as determinants of the behavioral actions of am-**

**phetamine in the rat. (Ph.D. dissertation).** Dissertation Abstracts International. 40(7):3473-B, 1980. Ann Arbor, Univ. Microfilms No. 7928594, 197p., 1979.

In three experiments on rats, the effects of amphetamine were examined under schedules which separated the usual relationship between response rate and rate of reinforcement in order to independently evaluate their roles in amphetamine action. The results of the three experiments are in agreement and support the hypothesis that the effects of amphetamine on schedule controlled operant behavior are determined by control rates of responding. Control rates of responding were found to determine the effects of amphetamine across a wide variety of circumstances and situations. It is reported that support for the rate dependency hypothesis was found under conditions where an alternative variable, rate of reinforcement, was also evaluated but was not found to contribute to the effects of amphetamine. (Journal abstract modified)

**003271** Luttges, Marvin W.; Gerren, Richard A. Dept. of Aerospace Engineering Sciences, University of Colorado, Boulder, CO 80309 **Postnatal alpha-methylphenylalanine treatment effects on adult mouse locomotor activity and avoidance learning.** Pharmacology Biochemistry and Behavior. 11(5):493-498, 1979.

Neonatal mice were injected for 5 days with a combination of alpha-methylphenylalanine and phenylalanine to determine the influences of excess phenylalanine during development on the behavior of these mice as adults. Spontaneous activity, bolus production, passsive avoidance learning, simple active avoidance learning, and complex active avoidance learning were tested in mice treated at two different postnatal periods. The results show that the treatments during development produced adult behavior alterations compared to controls. The effects were most pronounced in mice treated in the postnatal period immediately after birth. The behavioral effects can be summarized as increased emotionality and generalized, stimulus induced activity as well as decreased passive avoidance performance and complex activity avoidance performance. These behavioral deficits are consistent with those usually reported in various models of human phenylketonuria. 22 references. (Author abstract)

**003272** Lyness, W. H.; Friedle, N. M.; Moore, K. E. Dept. of Pharmacology and Toxicology, Michigan State University, East Lansing, MI 48824 **Destruction of dopaminergic nerve terminals in nucleus accumbens: effect on d-amphetamine self-administration.** Pharmacology Biochemistry and Behavior. 11(5):553-556, 1979.

The role of dopamine (DA) terminals in the nucleus accumbens in the self-administration of indirect acting DA agonists such as amphetamine and cocaine was studied. Control rates initiated self-administration of d-amphetamine and achieved stable injection rates within 7 to 10 days. Rats in which DA nerve terminals in nucleus accumbens were destroyed by bilateral microinjections of 6-hydroxydopamine (6-OHDA) did not initiate self-administraton of d-amphetamine when tested for as long as 19 days. In rates previously trained to self-administer d-amphetamine, 6-OHDA injections into nucleus accumbens abolished d-amphetamine self-administration. These results suggest tha DA nerve terminals in nucleus accumbens are necessary for both the acquisition and maintenance of d-amphetamine self-administration. 14 references. (Author abstract modified)

**003273** Macari, M.; Lico, M. C. Dept. of Morphology and Physiology, Veterinary School of Jaboticabal, 14870, Brazil **Nociceptive modulation in rats by chemical stimulation of caudate, septum and medial forebrain bundle.** Physiology & Behavior. 24(5):833-837, 1980.

The effects of intracerebral microinjections of thiopental (25mcg) and metrazol (100mcg) on the defensive motor responses elicited by nociceptive electrical stimulation of the tail were determined in male Holtzman rats. Thiopental had an antinociceptive action when injected in the medial septal area or medial forebrain bundle (MFB) and a hyperalgesic effect when injected into the caudate nucleus. Metrazol produced hyperalgesia when injected into the medial septal area or caudate nucleus and analgesia when injected into the MFB. Dopamine levels in the MFB and caudate nucleus and noradrenaline levels in the medial septal area were decreased after both drugs. 19 references. (Author abstract modified)

**003274** Madden, C.; Singer, G.; Oei, T. P. S. Dept. of Psychology, La Trobe University, Bundoora, Victoria, 3083, Australia **The involvement of interoceptive factors in the maintenance of heroin-seeking behavior.** Pharmacology Biochemistry and Behavior. 11(4):445-448, 1979.

The role of interoceptive stimuli in conditioned heroin seeking behavior was investigated in naive male Wistar rats. Animals self-injected heroin in saline solution for 21 days and were then allowed access to the original solution, saline only, distilled water, or no solution for 5 days. The operant rate of the heroin and heroin associated saline groups differed significantly from that of rats continually exposed to saline only. It is concluded that heroin seeking behavior was maintained in the heroin associated saline group by physiological conditioning following repeated association of saline and heroin. 21 references. (Author abstract modified)

**003275** Maes, Hugo. Laboratorium voor Neuro- en Psychofysiologie, Katholieke Universiteit te Leuven, Campus Gasthuisberg, Herestraat, B-3000 Leuven, Belgium **Time course and transition analysis of the behavioural effects of microinjection of pentobarbital and noradrenaline into the ventromedial hypothalamus of the rat.** Behavioural Processes. 4(4):341-358, 1979.

Effects of ventromedial hypothalamus (VMH) blockade with sodium pentobarbital (SPB) were examined. SPB blockade caused the emergence of feeding, the decrease in food transport and the drastic reduction of scanning. SPB enhances the occurence of sniffing into the litter immediately after the injection of SPB. Transitions toward sniffing litter became more preferred or less avoided after SPB than after either noradrenaline or food deprivation. With regard to the sequencing of behaviors, noradrenaline induced random chaining between behaviors, while SPB yielded a most rigid chaining and food deprivation produced an intermediate result. The data are matched against expectations from Veening's funnel model of behavior sequencing in VMH blocked rats. The relation between the enhancement of sniffing litter and of feeding after SPB is discussed. 23 references. (Author abstract modified)

**003276** Maes, Hugo. Laboratorium voor Neuro- en Psychofysiologie, Katholieke Universiteit te Leuven, Campus GHB, Herestraat, B-3000 Leuven, Belgium **Time course of feeding induced by pentobarbital-injections into the rat's VMH.** Physiology & Behavior. 24(6):1107-1114, 1980.

Eating induced in male Wistar rats by chemical blockade of the ventromedial hypothalamus (VMH) via single microinjections of pentobarbital did not outlast a 10 minute postinjection period. Very little feeding was observed when food was presented only after this period. Repeat injections after 10 and 20 minutes elicited eating, but the amount consumed decreased. Scanning behavior was depressed for 4 minutes after injection but recovered in 6 to 11 minutes. Sniffing was enhanced for 8 to 10 minutes. The limited meal size after VHM blockade appar-

ently resulted from diffusion of the anesthetic from the VMH. 22 references. (Author abstract modified)

**003277** Malick, Jeffrey B.; Enna, S. J. Biomedical Research Dept., Stuart Pharmaceuticals, Division of ICI Americas Inc., Wilmington, DE 19897 **Comparative effects of benzodiazepines and non-benzodiazepine anxiolytics on biochemical and behavioral tests predictive of anxiolytic activity.** Communications in Psychopharmacology. 3(4):245-252, 1979.

The comparative effects of benzodiazepines and nonbenzodiazepine anxiolytics on biochemical and behavioral tests predictive of anxiolytic activity were investigated. A significant correlation was found between potency as a displacer of 3H-diazepam binding and activity in the shock-induced suppression of drinking (SSD) tests in rats for 1,4 benzodiazepines. However, no correlation was found between activity in the neophobic-induced suppression of drinking (NSD) test and displacement of 3H-diazepam binding. Thus, although these two tests can predict anxiolytic activity with benzodiazepines, different neurochemical substrates may be involved. A significant correlation also existed between binding displacement and potency as anticonvulsants and for neuromuscular impairment (ataxia) among benzodiazepines. Thus, although displacement of 3H-diazepam binding may indicate anxiolytic potential, it may also detect properties that may be unrelated to antianxiety activity. Although the nonbenzodiazepine anxiolytics that were tested failed to displace 3H-diazepam binding, the anxiolytic activity of most of these agents was detected in the SSD test although not in the NSD procedure. Thus, the SSD test appears to be the best test for predicting anxiolytic activity with both benzodiazepines and structurally diversified compounds. 8 references. (Author abstract modified)

**003278** Manberg, P. J.; Nemeroff, C. B.; Prange, A. J., Jr. Dept. of Psychiatry, Biological Sciences Research Center, 220H, University of North Carolina, Chapel Hill, NC 27514 **Thyrotropin-releasing hormone and amphetamine: a comparison of pharmacological profiles in animals.** Progress in Neuro-Psychopharmacology. 3(4):303-314, 1979.

The pharmacological profiles of thyrotropin releasing hormone (TRH) and amphetamine are compared. A review of the literature indicates that the two substances not only share some common behavioral effects, but also show some obvious differences. It is concluded that the available data do not suggest a single mechanism of action underlying the behavioral effects of TRH. 65 references. (Author abstract modified)

**003279** Mantegazza, Paolo; Tammiso, Remigio; Vicentini, Lucia; Zambotti, Fernanda; Zonta, Nerina. Dept. of Pharmacology, School of Medicine, University of Milan, Milan, Italy **Muscimol antagonism of morphine analgesia in rats.** British Journal of Pharmacology. 67(1):103-107, 1979.

When administered intraventricularly to male Sprague-Dawley rats, the GABA receptor agonist muscimol antagonized the antinociceptive effect of centrally or systemically administered morphine. The antagonistic effect of muscimol on morphine analgesia was dose related and apparently linear. This finding supports the view that a GABA containing system is involved in morphine analgesia. 25 references. (Author abstract modified)

**003280** Margolin, David I.; Moon, Byong H. Moon: Department of Pharmacology, Rush-Presbyterian St. Luke's Medical Center, 1753 West Congress Parkway, Chicago, IL 60612 **Naloxone blockade of apomorphine-induced stereotyped behavior.** Journal of the Neurological Sciences. 43(1):13-17, 1979.

The effects of systematically administered naloxone on stereotyped behavior in the guinea-pig were investigated in order to elucidate a relationship between brain dopamine and the endogenous opiates. Systematic naloxone administration was found to block the production of stereotyped behavior induced by the direct dopamine agonist apomorphine. These results indicate that the endogenous opiates contribute to the production of stereotyped behavior initiated by dopaminergic stimulation and that endogenous opiates may function as central neurotransmitters with dopaminergic activity. 16 references. (Author abstract modified)

**003281** Margules, David L.; Goldman, Bruce; Finck, Alfred. Dept. of Psychology, Temple University, Philadelphia, PA 19122 **Hibernation: an opioid-dependent state? Brain Research** Bulletin. 4(6):721-724, 1979.

The role of endogenous opioids in hibernation was investigated in hamsters. Hibernation was found to substantially reduce heartrate, respiratory rate, body temperature, and arousal level. The heartrate was reversed dramatically by the injection of low doses of naloxone and in some cases the hamster aroused prematurely from hibernation. The effect is not due to the pain of the injection because saline injections did not produce such changes. The effect requires a preexisting state of hibernation because naloxone has no cardioacceleratory or arousal effect in nonhibernating hamsters that have had their heartrate and body temperature decreased substantially during hypothermia. These results suggest that endogenous opioids may contribute specifically to the state of hibernation. Moreover, a physiological role may exist for an antiopioid system in the promotion of arousal from hibernation. 6 references. (Author abstract modified)

**003282** Marini, James L.; Sheard, Michael H.; Kosten, Therese. Dept. of Psychiatry, Yale University School of Medicine, New Haven, CT 06510 **Study of the role of serotonin in lithium action using shock-elicited fighting.** Communications in Psychopharmacology. 3(4):225-233, 1979.

Shock elicited fighting was used as a model for the investigation of serotonergic mediation of lithium action. Chronic lithium diet resulted in decreased shock elicited fighting compared to control diet, but no difference in serotonin turnover. Chronic lithium treatment blocked the facilitory effect of lysergic acid diethylamide, or the inhibitory effect of chlorimipramine, on shock elicited fighting. Results are interpreted as significantly limiting possible tonic models of serotonergic mediation of lithium's effects. 34 references. (Author abstract modified)

**003283** Marks-Kaufman, Robin; Kanarek, Robin B. Kanarek: Dept. of Psychology, Tufts University, Medford, MA 02155 **Morphine selectively influences macronutrient intake in the rat.** Pharmacology Biochemistry and Behavior. 12(3):427-430, 1980.

Dietary self-selection of the three macronutrients (protein, carbohydrate, and fat) was examined in male rats following the administration of three doses of morphine sulphate (10, 15, and 30mg/kg). Intakes of all three macronutrients were suppressed in a dose dependent manner for a two hour period following morphine administration. Both protein and carbohydrate intakes remained suppressed for a six hour feeding period after morphine injections. In contrast, animals increased fat intake during the final four hours of the six hour feeding period resulting in an overall increase in fat intake. 16 references. (Author abstract)

**003284** Mason, Stephen T.; Fibiger, Hans C. Dept. of Psychiatry, University of British Columbia, Vancouver, British Columbia, Canada V6T 1W5 **Current concepts. I. Anxiety: the locus coeruleus disconnection.** Life Sciences. 25(26):2141-2147, 1979.

Recent research linking the noradrenergic nucleus locus coeruleus (LC) to a function in fear and anxiety is reviewed. Experiments are described using the selective catecholamine neurotoxin, 6-OHDA, to induce pharmacologically specific alteration in the functioning of noradrenaline (NA), which is released as a result of LC activity. These experiments examined the effects of forebrain NA depletion, alone and in conjunction with removal of the adrenal glands, on acquisition, retention, and extinction of one way active avoidance, on habituation to novelty, and on performance on previously learned two way active avoidance tasks. It was found that although electrolytic lesion to or electrical stimulation of LC in the monkey yields changes in fear behavior, more selective destruction on NA systems in the rat using 6-OHDA does not mimic this pattern. Possible explanations for the results are suggested. 67 references.

**003285** Mason, Stephen T.; Fibiger, Hans C. Division of Neurological Sciences, Dept. of Psychiatry, University of British Columbia, Vancouver, British Columbia V6T 1W5, Canada **The dorsal noradrenergic bundle and varieties of passive avoidance.** Psychopharmacology. 66(2):179-182, 1979.

The effects of lesion to the dorsal noradrenergic bundle on acquisition and retention of passive-avoidance learning were investigated in rats. Neither acquisition learning nor 24 hour retention was significantly altered by 6-OHDA intracerebral injections which depleted forebrain noradrenaline to less than 5% of control values. The absence of passive-avoidance impairment cannot be ascribed to functional recovery following the lesion since no impairment was found a mere 24 hours postoperatively nor in a strain of rat that does not show recovery in terms of noradrenaline sensitive adenylate cyclase. Nonassociative freezing to electric footshock, changed by the injections, resulted in slower acquisition at a footshock level of 4mA, but not at 1mA. The results are contrary to the predictions of the noradrenergic theory of learning. 19 references. (Author abstract modified)

**003286** Massotti, M.; Longo, V. G. Longo: Laboratorio di Farmacologia, Istituto Superiore di Sanita, Viale Regina Elena, 299, I-00161 Rome, Italy **Role of the dopaminergic system in the cataleptogenic action of bulbocapnine.** Journal of Pharmacy and Pharmacology. 31(10):691-695, 1979.

The time course for behavioral and biochemical effects of a cataleptogenic dose (50mg/kg i.p.) of bulbocapnine was determined in male Wistar rats. Catalepsy occurred immediately after drug injection and lasted for 1 hour. The onset of catalepsy was accompanied by a rise in homovanillic acid and 3,4-dihydroxyphenylacetic acid concentrations in whole brain and in discrete brain regions such as the striatum and limbic system. The dopamine content did not change in whole brain, but decreased in the striatum and increased in the cortex and hippocampus. No significant changes in noradrenaline, 5-hydroxytryptamine, or 5-hydroxyindoleacetic acid concentrations were observed. 35 references. (Author abstract modified)

**003287** Masur, Jandira; Boerngen, Roseli; Tufik, Sergio. Departamento de Psicobiologia, Escola Paulista de Medicina, Rua Botucatu, 862-04023 Sao Paulo, Brazil **Sex differences in the response to apomorphine in rats.** Pharmacology. 20(3):160-165, 1980.

Sex differences in the hypothermic and behavioral responses to apomorphine were studied in Wistar rats. Male rats showed more climbing behavior in response to apomorphine, whereas female rats showed a greater decrease in body temperature. Apomorphine-induced climbing behavior also increased with age in male rats. 14 references. (Author abstract modified)

**003288** Matsui, Yoshiki; Kamiok, Toshiharu. Central Research Laboratories, Sankyo Co., Ltd., Hiromachi 1-chome, Shinagawa-ku, Tokyo 140, Japan **Effects of intracerebral injection with muscimol on locomotor activity and catalepsy in rats.** Japanese Journal of Pharmacology. 29(3):496-499, 1979.

The locomotor and cataleptic effects of the GABA agonist muscimol were examined following injection of 100ng into various regions of the male Wistar-Imamichi rat brain. Injection of muscimol into the globus-pallidus-induced catalepsy and markedly decreased locomotor activity. Injection into the nucleus accumbens, amygdaloid nucleus, or caudate nucleus had no effect on catalepsy. Motor activity was slightly but significantly decreased after injection into the nucleus accumbens, but was not altered by injection into the amygdaloid or caudate nuclei. Results suggest that pallidal GABA mechanisms are involved in the inhibition of motor function. 14 references.

**003289** Matthews, William D.; Smith, Cynthia D. Dept. of Biological Research, Smith Kline and French Laboratories, Philadelphia, PA 19101 **Pharmacological profile of a model for central serotonin receptor activation.** Life Sciences. 26(17):1397-1403, 1980.

The head shake response in rats after systemic administration of the serotonin (5-HT) precursor 5-hydroxytryptophan (5-HTP) was pharmacologically characterized and shown to be a useful animal model to quantify brain 5-HT receptor activation. The behavior occurred in a dose dependent manner after injection of 5-HTP and the 5-HT agonist quipazine. Head shakes were also observed after injection of L-tryptophan, t-methoxydimethyltryptamine and fenfluramine. The 5-HT antagonists cyproheptadine and metergoline were potent blockers of the response. Xylamidine, a peripheral 5-HT antagonist, had no effect on head shaking. Inhibition of 5-HT uptake with fluoxetine potentiated the head shake response after 5-HTP. Manipulation of central cholinergic or GABAergic mechanisms did not alter 5-HTP-induced shakes. Alpha-noradrenergic receptor blockade had no significant effect on head shakes. However, desmethylimipramine was equipotent with methysergide as an antagonist of the behavior. Beta-noradrenergic receptor blockade had no specific effect on 5-HTP head shakes. Concomitant dopamine receptor activation with SK&F 38393 did not affect head shakes but the neuroleptics chlorpromazine and pimozide reduced the number of head shakes after 5-HTP. The H1 receptor antagonist pyrilamine had no effect on head shakes. It is concluded that 5-HTP-induced head shakes in rats is a quantitative model of brain 5-HT receptor activation which is particularly sensitive to 5-HT antagonists. 24 references. (Author abstract)

**003290** Mattingly, Bruce Adams. University of Kentucky **The role of cholinergic and serotonergic mechanisms in passive avoidance learning of the young domestic chick. (Ph.D. dissertation).** Dissertation Abstracts International. 40(11):5453-B, 1980. Ann Arbor, Univ. Microfilms No. 8010511, 198p., 1979.

The role of cholinergic and serotonergic mechanisms in passive avoidance learning of the young domestic chick was investigated, and the correlation between developmental changes in cholinergic and/or serotonergic functioning and the previously reported age dependent changes in passive avoidance learning between 1 and 4-day-old chicks was examined. In seven experiments, Vantress by Arbor Acre chicks were trained to key-peck for heat reinforcement when 4 days old, and then tested immediately for passive avoidance learning or resistance to extinction. Acute intraperitoneal injections of different doses of scopolamine and atropine or p-chlorophenylalanine (PCPA) were used to study cholinergic and serotonergic mechanisms, respectively. Results indicate: 1) that cholinergic, but not serotonergic mechanisms are involved in passive avoidance learning of the 4-day-old chick; and 2) that maturational changes in cholinergic mech-

anisms apparently cannot explain the age dependent changes in passive avoidance learning observed in the chick. (Journal abstract modified)

**003291** McCarten, M. D.; Lal, H. Dept. of Pharmacology and Toxicology, University of Rhode Island, Kingston, RI 02881 **Attenuation of the discriminative stimulus strength of morphine by haloperidol.** Neuropharmacology. 18(5):465-467, 1979.

The effects of haloperidol pretreatment on responding to morphine in a discrimination task were examined in male hooded Long-Evans rats. Animals weretrained to lever-press on a fixed-ratio 10 schedule of food reinforcement and to respond differentially on two levers while discriminating the effects of 10mg/kg morphine from the those of 1ml/kg saline. Pretreatment with haloperidol (0.32mg/kg) reduced the discriminability of morphine in these rats. Results suggest that reduction of narcotic self-administration by haloperidol may be due to its ability to markedly reduce the perception of the interoceptive stimuli produced by morphine. Since previous studies have shown that haloperidol potentiates the analgesic effects of morphine, these findings also suggest that the discriminative stimulus and analgesic properties of morphine may be based on different mechanisms. 18 references. (Author abstract modified)

**003292** McGee, David Henry, III. Northeast Louisiana University **Role of central catecholamines and 5-hydroxytryptamine in barbiturate withdrawal-induced audiogenic seizure in rats. (Ph.D. dissertation).** Dissertation Abstracts International. 40(9):4249-B, 1980. Ann Arbor, Univ. Microfilms No. 8005608, 113p., 1979.

The role of central catecholamines and 5-hydroxytryptamine (5-HT) in barbiturate withdrawal induced audiogenic seizure (AGS) in rats was investigated via pharmacological manipulation of norepinephrine (NE), dopamine (DA), and 5-HT functions. Selective depletion of catecholamines in rats was accomplished by administration of desipramine followed by intracerebroventricular injection of 6-hydroxydopamine (6-OHDA). Animals receiving both drugs were depleted only of DA whereas those receiving only 6-0HDA were depleted of both catecholamines. Intracerebroventricular administration of NE to rats was found to decrease susceptibility to AGS. Depletion of 5-HT by p-chlorophenylalanine caused significant enhancement of withdrawal-induced AGS severity, though susceptibility was unaltered. Results suggest that both NE and 5-HT, but not DA may be important in the modulation of severity of the barbiturate withdrawal-induced audiogenic seizure. (Journal abstract modified)

**003293** McGlone, John J.; Ritter, Sue; Kelley, Keith W. Kelley: Animal Sciences Dept., Washington State University, Pullman, WA 99164 **The antiaggressive effect of lithium is abolished by area postrema lesion.** Physiology & Behavior. 24(6):1095-1100, 1980.

Thermal lesions of the area postrema abolished the ability of lithium (Li) to condition taste aversions in Sprague-Dawley rats. Area postrema lesions also abolished the antiaggressive effect of Li, as measured by attack latency in a shock-induced aggression test. Results suggest that some or all of the antiaggressive effects of Li in rats may be due to malaise induced by Li's action on the area postrema. 38 references. (Author abstract modified)

**003294** McKim, W. A. Dept. of Psychology, Memorial University of Newfoundland, St. John's, Newfoundland, Canada A1B 3X9 **The effects of scopolamine on three different types of suppressed behavior of rats.** Pharmacology Biochemistry and Behavior. 12(3):409-412, 1980.

The effects of scopolamine on three different types of suppressed behavior of rats were investigated. Twelve albino rats were trained to lever-press on a variable-interval one minute schedule (VI1) for sweetened condensed milk reinforcement. While responding on this schedule, a two minute tone was presented. For one group it signalled a response contingent shock (punishment), for another group it signalled the delivery of an unavoidable noncontingent shock at its termination (CER) and for a third group, reinforcement was withheld during the tone (extinction). In the first experiment, scopolamine in doses of 0.8 to 12.8mg/kg did not alter response rates during the tone for any group. In a second experiment, 16 hooded rats were tested with 6.4mg/kg of scopolamine using a similar procedure, but with different shock levels, apparatus, reinforcement and session duration. For all three groups, the drug depressed responding during the tone. It is concluded that when all other aspects of the situation are equated, scopolamine will produce the same effect on behavior suppressed by punishment, CER, and extinction. 9 references. (Author abstract modified)

**003295** McKim, William A. Psychology Dept., Memorial University of Newfoundland, St. John's, Newfoundland A1B 3X9, Canada **The effect of caffeine, theophylline and amphetamine on operant responding of the mouse.** Psychopharmacology. 68(2):135-138, 1980.

Caffeine, theophylline, and d-amphetamine were given to C57BL mice responding on a multiple fixed-interval (FI) 10 minute, fixed-ration (FR) 30 schedule for evaporated milk. All three drugs increased FI rates of responding at nearly the same molar dose, with amphetamine the most effective and caffeine the least. Intermediate doses of amphetamine severely decreased FR rates of responding but increased FI rates of responding. High doses of the methylxanthines decreased FI and FR rates. The effects of all three drugs were rate dependent. 13 references. (Author abstract modified)

**003296** McNaughton, N.; Feldon, J. Dept. of Experimental Psychology, South Parks Road, Oxford, England **Spontaneous alternation of body turns and place: differential effects of amylobarbitone, scopolamine and septal lesions.** Psychopharmacology. 68(2):201-206, 1980.

Amylobarbitone, scopolamine, and medial and lateral septal lesions had differential effects on spontaneous alternation in male Wistar or Sprague-Dawley rats, possibly as a result of their differing effects on the hippocampal theta rhythm. Scopolamine (1.2mg/kg i.p.) reduced both body turn alternation and place alternation, but amylobarbitone (20mg/kg i.p.) reduced only the alternation of body turns. Medial septal lesions produced significant perserveration of body turns and a nonsignificant reduction in place alternation. Lateral septal lesions had no apparent effect on alternation. 19 references. (Author abstract modified)

**003297** Means, Larry W.; Franklin, Ronald D.; Cliett, Charles E. Dept. of Psychology, East Carolina University, Greenville, NC 27834 **Failure of piracetam to facilitate acquisition or retention in younger or older rats.** Experimental Aging Research. 6(2):175-180, 1980.

The performance of Long-Evans rats of two age groups (450 and 75 days) was observed in open-field activity, one way active avoidance and passive avoidance conditioning. One half of the Ss in each group were given 100mg/kg of piracetam 2 hours prior to all tests. Younger Ss required fewer acquisition trials to reach active avoidance criterion and made more active avoidances on 7 day retention tests than older Ss. Thus, younger Ss performed better on both acquisition and retention of active and passive avoidance conditioning. Piracetam did not produce significant behavioral changes in any of the groups on

any of the tasks. Neither age nor piracetam affected activity. 19 references. (Author abstract modified)

**003298** Megens, Anton A. P. H.; Cools, A. R. Dept. of Pharmacology, University of Nijmegen, P.O. Box 9101, 6500 HB Nijmegen, The Netherlands **Effects of intraseptal administration of cholinergic agents on morphine-induced behavior of cats.** Psychopharmacology. 66(2):183-188, 1979.

Behavioral effects of intraseptal administration of cholinergic agents were analyzed in cats pretreated with morphine 15 to 20 minutes or 40 minutes earlier. Carbachol and scopolamine given 15 to 20 minutes after morphine accelerated and retarded, respectively, the normal development of the morphine syndrome. Carbachol resulted in the display of stereotyped and ritualized patterns, i.e., symptoms characteristic of cats pretreated 30 to 40 minutes earlier with morphine, whereas scopolamine reduced the frequency of the behavioral items in comparison with controls, and retarded the onset of stereotyped and ritualized patterns. Carbachol given 40 minutes after morphine increased the frequency of stereotyped and ritualized patterns displayed at that time. This dose dependent effect, mimicked by arecoline and the combination of acetylcholine and physostigmine, could be antagonized by atropine and scopolamine, which per se had no influence on the stereotyped and ritualized patterns. It is concluded that the degree of cholinergic muscarinic activity within the septal nuclei at least partly determines the genesis of the morphine syndrome in cats. The data are discussed in view of the hypothesis that systemically administered morphine and intraseptally applied cholinergic agents affect the cholinergic septo/hippocampal system in a common way via distinct sites of action at the level of the septal nuclei. 27 references. (Author abstract modified)

**003299** Meldrum, Brian; Horton, Roger. Dept. of Neurology, Institute of Psychiatry, De Crespigny Park, SE5 8AF, England **Effects of the bicyclic GABA agonist, THIP, on myoclonic and seizure responses in mice and baboons with reflex epilepsy.** European Journal of Pharmacology. 61(3):231-237, 1980.

The anticonvulsant effects of 4,5,6,7-tetra hydroisoxazolo (5,4-C) pyridine-3-ol (THIP) were tested in DBA/2 mice with audiogenic seizures and in baboons with photosensitive epilepsy. In mice, no protection against seizures was afforded by 1 to 4mg/kg i.p. THIP, but a dose of 8mg/kg reduced clonic and seizure responses. The 8mg/kg dose also reduced rectal temperature and impaired posture and spontaneous activity. In baboons, 0.25 to 8mg/kg i.v. THIP failed to protect against photically-induced myoclonic responses. Toxic signs, including focal or generalized myoclonus, were observed at the 8mg/kg dose. It is concluded that THIP is not effective against reflex epilepsy. 25 references. (Author abstract modified)

**003300** Mele, Paul Camille. Adelphi University **A behavioral analysis of serotonin antagonists and their interaction with D-amphetamine. (Ph.D. dissertation).** Dissertation Abstracts International. 40(12):5860-B, 1980. Ann Arbor, Univ. Microfilms No. 8012521, 197p., 1980.

The effects of serotonin antagonists methysergide and cinanserin on multiple schedule responding of rats and the interactive effects of these serotonin antagonists with d-amphetamine on multiple schedule responding were investigated. In Experiment 1, and multiple fixed-interval 2 min differential reinforcement of low rate 18 sec schedule of sweetened mild delivery (mult FI DRL) was used to maintain responding in rats. Following the combined administration of d-amphetamine with methysergide or cinanserin, FI response rates were typically reduced relative to those obtained with d-amphetamine alon. For DRL responding, the drug combination produced potentiated rate increases at the low doses of d-amphetamine; rate increases at the low doses of d-amphetamine; at the higher d-amphetamine dose combinations the rate increasing effects of d-amphetamine alone were attenuated. In a mult FI 2 min FI 2 min schedule in which one component was consistently punished, chlordiazepoxide frequently increased punished responding to a greater degree than comparable rates of unpunished responding. It is suggested that serotonin antagoisms may be the mechanisms underlying the effects of methysergide reported here. (Journal abstract modified)

**003301** Meltzer, Leonard T.; Rosecrans, John A.; Aceto, Mario D.; Harris, Louis S. Rosecrans: Dept. of Pharmacology, Medical College of Virginia, Richmond, VA 23298 **Discriminative stimulus properties of the optical isomers of nicotine.** Psychopharmacology. 68(3):283-286, 1980.

The stereospecificity of the central nicotinic receptor that mediates the stimulus effect of nicotine was studied. In male Sprague-Dawley rats trained to discriminate 200 or 400mcg/kg (-)-nicotine from saline, (-)-nicotine was nine times more potent than ()-nicotine. Mecamylamine blocked the cues of the two nicotine isomers equally. Hexamethonium and atropine had no effect. 11 references. (Author abstract modified)

**003302** Miceli, Dom; Marfaing-Jallat, Pierrette; Le Magnen, Jacques. Lab. de Neurophysiologie Sensorielle et Comportementale, College de France 11, place Marcelin Berthelot, F-75231 Paris Cedex 05, France **Non-specific enhancemant of ethanol-induced taste aversion by naloxone.** Pharmacology Biochemistry and Behavior. 11(4):391-394, 1979.

The conditioned taste aversion (CTA) paradigm was used to examine the effect of naloxone on ethanol-induced aversion to a saccharin solution in male Wistar rats. Naloxone itself produced no aversion to the saccharin flavor, but the narcotic antagonist significantly enhanced CTA induced by ethanol or by lithium chloride. These findings are compatible with a role for opiates in modulating pain and with a hypernociceptive action for naloxone. 31 references. (Author abstract modified)

**003303** Miyamoto, Masaomi; Narumi, Shigehiko; Nagai, Yasuo; Shima, Takashi; Nagawa, Yuji. Medicinal Research Laboratories, Central Research Division, Takeda Chemical Industries, Ltd., Osaka 532, Japan **Thyrotropin-releasing hormone: hyperactivity and mesolimbic dopamine system in rats.** Japanese Journal of Pharmacology. 29(3):335-347, 1979.

Thyrotropin releasing hormone (TRH) produced significant hyperactivity when injected i.p. (20mg/kg) or bilaterally (10mcg) into the nucleus accumbens septi (NAS) of male Sprague-Dawley rats. Bilateral injection of 6-hydroxydopamine into the mesolimbic dopamine (DA) pathway did not alter the hyperactivity induced by TRH, but enhanced the response to i.p. apomorphine or intraaccumbens DA. The TRH-induced hyperactivity was suppressed by alpha-methyltyrosine and augmented by pargyline. The stimulatory effect of TRH was also markedly reduced by systemic injection of aminooxyacetic acid in a dose that itself produced behavioral depression. Ethanolamine O-sulfate (100mcg) injected bilaterally into the NAS had no behavioral depressant effect itself, but markedly attenuated the hyperactivity induced by central or peripheral administration of TRH or DA. TRH and methamphetamine both increased the spontaneous release of radiolabeled DA from rat NAS slices. Results suggest that TRH induces hyperactivity by enhancing DA release from nerve terminals in the NAS, rather than by direct stimulation of postsynaptic DA receptors. TRH and GABA may play a reciprocal role in regulating the activity of mesolimbic DA neurons. 35 references. (Author abstract modified)

**003304** Moerschbaecher, Joseph M.; Thompson, Donald M. Dept. of Pharmacology, Georgetown University Schools of

Medicine and Dentistry, Washington, DC 20007 **Effects of d-amphetamine, cocaine, and phencyclidine on the acquisition of response sequences with and without stimulus fading.** Journal of the Experimental Analysis of Behavior. 33(3):369-381, 1980.

The effects of d-amphetamine, cocaine, and phencyclidine on the acquisition of response sequences with and without stimulus fading were investigated. In each of three components of a multiple schedule, monkeys were required to emit a different sequence of four responses in a predetermined order on four levers. Sequence completions produced food on a fixed-ratio schedule. Errors produced a brief timeout. One component of the multiple schedule was a repeated acquisition task where the four response sequence changed each session (learning). The second component of the multiple schedule was also a repeated acquisition task, but acquisition was supported through the use of a stimulus fading procedure (faded learning). In a third component of the multiple schedule, the sequence of responses remained the same from session to session (performance). At higher doses, d-amphetamine, cocaine, and phencyclidine decreased the overall rate of responding and increased the percent errors in all three components. At lower doses, however, the three drugs produced selective effects on errors. Errors were increased in the learning component at lower doses than those required to disrupt the behavior in the faded learning component. The performance component tended to be the least sensitive to disruptive drug effects. The data are consistent with the view that stimulus fading can modulate the effects of drugs on acquisition. 23 references. (Author abstract modified)

**003305** Mogilnicka, E.; Klimek, V. Institute of Pharmacology, Polish Academy of Sciences, 12, Smetna-Str., 31-343 Krakow, Poland **Mianserin, danitracen and amitriptyline withdrawal increases the behavioural responses of rats to L-5-HTP.** Journal of Pharmacy and Pharmacology. 31(10):704-705, 1979.

The behavioral response to 1-5-hydroxytryptophan (L-5-HTP, 12.5mg/kg i.p.) was examined in male Wistar rats following repeated administration of mianserin and danitracen, antidepressant drugs that block 5-hydroxytryptamine (5-HT) receptors, or amitriptyline, a tricyclic antidepressant that inhibits uptake of 5-HT and noradrenaline. A single 2mg/kg dose of mianserin did not affect the number of head shakes induced by L-5-HTP, but 4 day administration elevated the number of shakes seen after withdrawal. A single 3mg/kg dose of danitracen increased the number of shakes induced by L-5-HTP; a similar but much stronger effect was seen 72 hours after termination of 4 or 10 day danitracen treatment. A single 10mg/kg dose of amitrityline had no effect on L-5-HTP-induced shakes, but 4 and 10 day treatments increased the number of shakes. The enhanced response to L-5-HTP in animals treated chronically with mianserin or danitracen was marked 72 hours after withdrawal but was not observed 24 hours after withdrawal, suggesting the response was due to prolonged blockade of 5-HT receptors. 14 references.

**003306** Montanaro, N.; DallOlio, R.; Gandolfi, O. Institute of Pharmacology, University of Bologna, Bologna, Italy **Bromolysergide and methysergide protection against ECS-induced retrograde amnesia.** Neuropsychobiology. 5(3):174-180, 1979.

Bromolysergide (BOL 148) and methysergide (UML 491) protection against electroconvulsive shock (ECS)-induced retrograde amnesia was investigated. BOL 148 and UML 491 were administered to rats 45 minutes before one trial passive avoidance conditioning followed by ECS or sham ECS. On test session (24 hours later), the groups treated with both BOL 148 and UML 491 exhibited a clear cut retention in comparison to saline ECS rats. On the other hand, all drugged groups, regardless of their submission to ECS, showed a little less pronounced consolidation than saline ECS rats. The antiamnestic effect brought about by the two drugs is discussed in terms of receptor antagonism against ECS released brain serotonin, whereas the lower passive avoidance level observed in treated animals is considered in relation to a possible antipunishment effect of antiserotoninergic treatment. 24 references. (Author abstract modified)

**003307** Monti, J. M. Dept. of Pharmacology and Therapeutics, Hospital de Clinicas P1, Montevideo, Uruguay **The effects of neuroleptics with central dopamine and noradrenaline receptor blocking properties in the L-DOPA and ()-amphetamine-induced masking EEG in the rat.** British Journal of Pharmacology. 67(1):87-91, 1979.

The role of noradrenaline (NA) and dopamine (DA) in the increased EEG arousal induced by ()-amphetamine or l-DOPA in male Wistar rats was examined. Haloperidol (0.6mg/kg), which blocks receptors for both catecholamines, reversed the EEG desynchronizing actions of l-DOPA and amphetamine. Low doses of pimozide (0.4 to 0.8mg/kg) that block only DA receptors did not modify the drug-induced EEG changes, but a 1mg/kg dose, which also blocks NA receptors, counteracted the increase in waking elicited by amphetamine. Spiroperidol (1 to 4mg/kg), a specific DA receptor blocker, had no effect on the arousal induced by l-DOPA or amphetamine. Results suggest that the increased waking time induced by the catecholamine agonists was related to an increased availability of NA rather than DA. 16 references. (Author abstract modified)

**003308** Moon, Byong H.; Feigenbaum, Jeffery J.; Carson, Paul E.; Klawans, Harold L. Dept. of Neurological Science, Rush-Presbyterian-St. Luke's Medical Center, Congress Parkway, Chicago, IL 60612 **The role of dopaminergic mechanisms in naloxone-induced inhibition of apomorphine-induced stereotyped behavior.** European Journal of Pharmacology. 61(1):71-78, 1980.

Naloxone (NX) inhibited apomorphine-induced stereotyped behavior (AISB) in male Sprague-Dawley rats and acted synergistically with subthreshold doses of haloperidol to produce the same effect. However, NX was not able to totally abolish AISB and could not inhibit this response at any dose by more than half the stereotypy rating for apomorphine injected control rats. Animals given 0.20 to 20.0mg/kg NX continued to exhibit sniffing, head movements, and other low intensity components of stereotypy, but licking and biting were abolished. In contrast, a 0.20mg/kg dose of haloperidol completely abolished AISB. 32 references. (Author abstract modified)

**003309** Mora, F.; Alba, F.; Sanguinetti, A. M.; Rodriguez, J. M.; Vives, F. Dept. of Physiology, School of Medicine, University of Granada, Granada, Spain **Differential effects produced by an anticholinergic on the neuroleptic inhibition of motor behaviour and self-stimulation of the prefrontal cortex in the rat.** Brain Research Bulletin. 5(3):223-225, 1980.

The dopamine receptor blocker spiroperidol (0.016 to 0.128mg/kg i.p.) produced a dose related inhibition of spontaneous motor activity and of self-stimulation of the medial prefrontal cortex in male Sprague-Dawley rats. The anticholinergic drug dexetimide (0.5 or 1.0mg/kg) antagonized the motor impairment induced by spiroperidol but caused a decrease in prefrontal cortex stimulation. Results support the proposed role of dopamine in self-stimulation of the prefrontal cortex in the rat. 15 references. (Author abstract modified)

**003310** Morelli, Micaela; Porceddu, Maria Luisa; Di Chiara, Gaetano. Di Chiara: Institute of Pharmacology, University of Cagliari, Cagliari, Italy **Lesions of substantia nigra by kainic acid: effects on apomorphine-induced stereotyped behaviour.** Brain Research. 191(1):67-78, 1980.



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Apomorphine-induced stereotypy was examined in male Sprague-Dawley rats 15 days after bilateral kainic acid lesions of the substantia nigra. Low doses (0.1 and 0.2mg/kg) of apomorphine induced similar increases in motility and sniffing in lesioned and control animals. After larger doses (1.0 and 2.5mg/kg), sniffing was observed in lesioned animals instead of the gnawing seen in controls. Bilateral infusion of kainic acid into the reticular formation 2.0mm dorsal to the substantia nigra had no effect on apomorphine-induced stereotypy. Results suggest that the substantia nigra mediates motor and behavioral syndromes of striatal origin through nondopaminergic pars reticulata neurons. 36 references. (Author abstract modified)

**003311** Moss, Donald E.; Johnson, Richard L. Dept. of Psychology, University of Texas, El Paso, TX 79968 **Tonic analgesic effects of delta9-tetrahydrocannabinol as measured with the formalin test.** European Journal of Pharmacology. 61(3):313-315, 1980.

The analgesic effects of delta9-tetrahydrocannabinol (THC) were evaluated in the formalin test. Rats were given 5 or 10mg/kg THC or placebo by gavage 4 hours prior to testing. THC provided significant analgesia against tonic and phasic pain and may have therapeutic value when used with another analgesic or potentiating drug. 8 references. (Author abstract modified)

**003312** Munoz, Carmen; Grossman, Sebastian P. Grossman: University of Chicago, 5848 South University Avenue, Chicago, IL 60637 **Behavioral consequences of selective destruction of neuron perikarya in septal area of rats.** Physiology & Behavior. 24(4):779-788, 1980.

Behavioral consequences of selective destruction of neuron perikarya in septal area of rats with kainic acid (KA) were investigated. KA resulted in significant depletion of neurons in medial septum, while the lateral septum was entirely intact (n=7), or affected only unilaterally (n=7) by these injections. Selective destruction of neurons indigenous to the septal area reproduced some but not all of the behavioral effects of septal lesions. KA injections produced transient hyperdipsia and hyperphagia, as well as marked disinhibitory effects on punished licking (passive avoidance) but failed to affect shuttle box avoidance, sucrose or saline preference, or locomotor activity in a novel environment. 70 references. (Author abstract modified)

**003313** Murray, Thomas Francis. University of Washington **Phencyclidine: a behavioral, dispositional and neurochemical evaluation in the rat. (Ph.D. dissertation).** Dissertation Abstracts International. 40(7):3113-B, 1980. Ann Arbor, Univ. Microfilms No. 7927848, 186p., 1979.

The effects of acute and chronic administration of phencyclidine were examined in rats trained to respond on a water reinforced VI-60 schedule. The acute administration of phencyclicidine in doses of 0.25, 0.5, and 1.0mg/kg increased the mean response rates, respectively, to 1.18, 1.40, and 1.43 times the control rate. In contrast, doses of 2.0 and 4.0mg/kg decreased the response rates to 73 and 6% of the respective control rates. After 7 daily injections of 4mg/kg, complete tolerance developed to the rate depressant effects of phencyclidine; this tolerance was not related to behavioral compensatory mechanisms. Also investigated were: the relationship between the brain levels of phencyclidine and its behavioral effects; the role of dispositional mechanisms in the observed tolerance as determined by comparing the cerebral disposition of phencyclidine in acutely and chronically treated rats; and the phencyclidine-induced stereotyped behavioral syndrome in rats. Finally, the effects of phencyclidine on striatal dopamine turnover are assessed by measurement of the decline in dopamine concentration after inhibition of tyrosine hydroxylase with alpha MPT. (Journal abstract modified)

**003314** Myers, B. M.; Baum, M. J. Baum: Room 37-315, Massachusetts Institute of Technology, Cambridge, MA 02139 **Facilitation of copulatory performance in male rats by naloxone: effects of hypophysectomy, 17alpha-estradiol, and luteinizing hormone releasing hormone.** Pharmacology Biochemistry and Behavior. 12(3):365-370, 1980.

Three experiments exploring the mechanisms whereby systemic administration of the opiate receptor antagonist, naloxone hydrochloride causes reductions in the frequency of intromissions preceding ejaculation and latency to ejaculation in sexually experienced male rats, are described. Administration of naloxone to male rats which were hypophysectomized in addition to being castrated and implanted with capsules containing testosterone caused such behavioral changes, suggesting that these behavioral effects of naloxone do not result from interference with the binding of endorphin of pituitary origin. Surprisingly, a significant facilitatory effect of naloxone on sexual performance was absent in castrated controls bearing testosterone implants. Recent evidence suggests that 17alpha-hydroxylated estrogens, which may be produced in gonadally intact males, possess appreciable affinity for opioid receptors. However, daily administration of 17alpha-estradiol to castrated, testosterone implanted males failed to make them as behaviorally responsive to naloxone as gonadally intact animals. Administration of luteinizing hormone releasing hormone (LHRH) caused a significant reduction in ejaculation latency in gonadally intact males but not in castrated males bearing testosterone implants. It is suggested that the facilitatory effect of naloxone on masculine sexual performance results, in part, from a drug-induced release of LHRH. 32 references. (Author abstract modified)

**003315** Myslobodsky, M. S.; Ackermann, R. F.; Golovchinsky, V.; Engel, J., Jr. Psychobiology Research Unit, Dept. of Psychology, Tel-Aviv University, Tel-Aviv, Israel **Ketamine-induced rotation: interaction with GABA-transaminase inhibitors and picrotoxin.** Pharmacology Biochemistry and Behavior. 11(5):483-486, 1979.

A systematic assessment was sought of the effects of recently synthesized GABA-transaminase (GABA-T) inhibitors, gamma-vinyl GABA and gamma-acetylenic GABA, and a GABA antagonist, picrotoxin, on ketamine anesthesia. Ketamine in a dose of 100 mg/kg produced stereotypic behavior and vigorous rotation in adult male rats, consisting of a short first rotation phase, an anesthetic phase lasting 20 to 30 minutes, and a second rotation period. A single dose of either GABA-T inhibitor 4 hours prior to ketamine shortened the first rotation phase, increased the anesthetic phase, changed the pattern of postanesthetic rotation, and reduced total and net rotation scores. Picrotoxin given 10 minutes prior to ketamine tended to act in the opposite direction although none of its effects reached statistical signifiance. Results are discussed in regard to metabolism of major transmitters such as dopamine and norepinephrine, and in relation to suggestions that ketamine produces a model of some aspects of schizophrenia and that, thus, GABA-T inhibitors may have an antipsychotic effect. 28 references. (Author abstract modified)

**003316** Nakano, Shigeyuki; Hara, Chiaki; Ogawa, Nobuya. Dept. of Pharmacology, Ehime University, School of Medicine, Shigenobu-Cho Onsen-Gun, Ehime-Ken 791-02 Japan **Circadian rhythm of apomorphine-induced stereotypy in rats.** Pharmacology Biochemistry and Behavior. 12(3):459-461, 1980.

The existence of circadian variations of apomorphine-induced stereotypy was determined in male Wistar rats. Ss were standardized to a light/dark cycle (lights on from 7:00 to 19:00) for 3

weeks and injected with apomorphine hydrochloride at one of six times (9:00, 13:00, 17:00, 21:00, 1:00 and 5:00). A significant time of day effect was found for apomorphine-induced stereotypy, with highest stereotypic score following injection at 13:00 or 17:00. The circadian rhythm of apomorphine-induced stereotypy was significantly fitted to a single cosine curve with a 24 hr cycle using the least squares method. 15 references. (Author abstract modified)

**003317** Nash, Richard F.; Newton, Debra K. Dept. of Psychology, Marquette University, Milwaukee, WI 53233 **Effect of neurotransmitter reuptake blockers on tonic immobility in chickens.** Bulletin of the Psychonomic Society. 15(4):279-281, 1980.

The effects of two neurotransmitter reuptake blockers, nisoxetine and fluoxetine, on the tonic immobility (TI) response were examined in chickens. Nisoxetine was found to diminish significantly both the duration of the TI response and the number of inductions needed to elicit it. Fluoxetine was found to have no significant effect on either the duration of TI or the number of inductions needed to elicit it. It is suggested that additional research with fluoxetine is necessary, with the possible use of an intraventricular route for administration of the drug. 13 references. (Author abstract modified)

**003318** Nazzaro, Jules; Gardner, Eliot L. Gardner: Dept. of Psychiatry, Albert Einstein College of Medicine, Bronx, NY 10461 **GABA antagonism lowers self-stimulation thresholds in the ventral tegmental area.** Brain Research 189(1):279-283, 1980.

The effects of the GABA antagonist picrotoxin and the opiate antagonist naloxone on the intracranial self-stimulation (ICSS) elicited from the A-10 dopaminergic nucleus in male Sprague-Dawley rats were examined. Picrotoxin (1.0mg/kg i.p.) significantly lowered the ICSS threshold 10 and 40 minutes after injection. Naloxone (5mg/kg i.p.) did not alter the ICSS threshold and did not affect the picrotoxin-induced decrease in ICSS threshold. Results suggest the presence of an inhibitory GABA synaptic input to mesolimbic/mesocortical neurons subserving ICC in the A-10 ventral tegmental area. This GABAergic modulation of A-10 dopamine neurons does not appear to be medicated through enkephalinergic neurons. 32 references.

**003319** Nicholson, A. N.; Wright, Catherine M. Royal Air Force Institute of Aviation Medicine, Farnborough, Hampshire, England **Comparative studies with thieno- and benzodiazepines: spatial delayed alternation behaviour in the monkey (Macaca mulatta).** Neuropharmacology. 19(5):491-494, 1980.

The effects of benzodiazepines (temazepam, nordiazepam, and clobazam) and triazolo-1,4-thienodiazepines (brotizolam and WE-973) on spatial delayed alternation in monkeys were compared. With i.p. doses of 0.5 to 3.0mg/kg, nordiazepam reduced the total number of correct responses and the thienodiazepines reduced the number of correct responses and increased total response time; temazepam and clobazam had no effect. At doses ranging from 5.0 to 25.0mg/kg, temazepam reduced the number of correct responses and increased total response time, but clobazam still had no effect. 29 reference. (Author abstract modified)

**003320** Nielsen, Erik B.; Lee, Tong H.; Ellison, Gaylord. Research Lab., Dept. E, Sct. Hans Hospital, DK-4000 Roskilde, Denmark **Following several days of continuous administration d-amphetamine acquires hallucinogenlike properties.** Psychopharmacology. 68(2):197-200, 1980.

Limb flicks and whole body shakes were observed in rats treated acutely with lysergic acid diethylamide or mescaline and in those pretreated for 108 hours with a slow release d-aphetamine pellet, given a 12 hour rest period, and then injected with d-amphetamine. The amphetamine treated animals also showed excessive grooming of the body surface. It is suggested that the behavioral syndrome induced by continuous amphetamine administration can serve as an animal model of the amphetamine psychosis induced by a similar drug regimen in humans. 17 references. (Author abstract modified)

**003321** Nieto, Javier, Makhlouf, Cesar; Rodriguez, Rodolfo. Departamento de Farmacologia, Facultad de Medicina, Universidad Nacional Autonoma de Mexico, Apdo. Postal 70-297, Mexico 20 **d-Amphetamine effects on behavior produced by periodic food deliveries in the rat.** Pharmacology Biochemistry and Behavior. 11(4):423-430, 1979.

Activities were monitored in food deprived rats given milk every 60 seconds, then food satiated and exposed to the fixed-time reinforcement schedule a second time. Results indicate that d-amphetamine increased food tray directed activities, reduced grooming, and had mixed effects on rearing and sniffing. In a second experiment with rats given a food pellet every 60 seconds and allowed to drink water, d-amphetamine increased time spent in contact with the food tray but reduced time spent drinking, grooming, rearing, and sniffing. Results suggest that d-amphetamine facilitates tray directed activities and produces a corresponding reduction in competing activities. 27 references. (Author abstract modified)

**003322** Nomura, Y.; Segawa, T. Dept. of Pharmacology, Institute of Pharmaceutical Sciences, Hiroshima University School of Medicine, Kasumi 1-2-3, Hiroshima 734, Japan **The effect of alpha-adrenoceptor antagonists and metiamide on clonidine-induced locomotor stimulation in the infant rat.** British Journal of Pharmacology. 66(4):531-535, 1979.

Pretreatment with the alpha-adrenoceptor antagonists phenoxybenzamine, yohimbine, or piperoxan significantly reduced the forward locomotion and wall climbing induced in 7-day-old Wistar rats by clonidine. The clonidine-induced locomotor stimulation was not affected by metiamide, a histamine H2-receptor blocker. Results suggest that central alpha-adrenoceptors may be involved in clonidine-induced locomotor stimulation, but histamine H2-receptors are not 24 references. (Author abstract modified)

**003323** Nomura, Yasuyuki; Oki, Keiko; Segawa, Tomio. Dept. of Pharmacology, Institute of Pharmaceutical Sciences, Hiroshima University School of Medicine, Kasumi 1-2-3, Hiroshima 734, Japan **Pharmacological characterization of central alpha-adrenoceptors which mediate clonidine-induced locomotor hypoactivity in the developing rat.** Naunyn-Schmiedeberg's Archives of Pharmacology. 311(1):41-44, 1980.

Clonidine produced locomotor hyperactivity in 7-day-old Wistar rats and hypoactivity in 20-day-old rats. Phenoxybenzamine decreased spontaneous activity in a dose dependent manner, but did not antagonize the clonidine-induced hypoactivity in 20-day-old rats. Pretreatment with phentolamine, yohimbine, or piperoxan in doses that did not cause hypoactivity did block the clonidine-induced hypoactivity. Results suggest that clonidine may induce locomotor hypoactivity by activating presynaptic alpha2 adrenoceptors in the CNS of 20-day-old rats. 17 references. (Author abstract modified)

**003324** Nyakas, C.; Bohus, B.; De Wied, D. Bohus: Rudolf Magnus Institute for Pharmacology, Vondellaan 6, 3521 GD Utrecht, The Netherlands **Effects of ACTH4-10 on self-stimulation behavior in the rat.** Physiology & Behavior. 24(4):759-764, 1980.

The threshold current evoking self-stimulation or multiples of this current were used to investigate the effect of ACTH4-10 on

response performance for brain stimulation reward in the medial septum (MS) and the medial forebrain bundle (MFB) in the rat. ACTH4-10 in a dose of 50mcg administered subcutaneously enhanced bar-pressing for low intensity stimulation but failed to change self-stimulation rates when the baseline rate exceeded 100 responses per 6 minutes. The peptide lowered the threshold for producing self-stimulation but only in the MS. When an ascending sequence of threshold multiples was used within a session, ACTH4-10 treatment resulted in an increase in response rate at 1.2 and 1.5 threshold multiples and a decrease at 3.0 times the threshold but only in the MS. The results indicate that ACTH4-10 facilitates response performance at a low response rate by enhancing the rewarding effect of brain stimulation. Furthermore, the peptide changed the response pattern which normally follows reinforcement shift in the MS. 36 references. (Author abstract modified)

**003325** ODonnell, James M.; Miczek, Klaus A. Miczek: Dept. of Psychology, Tufts University, Medford, MA **No tolerance to antiaggressive effect of d-amphetamine in mice.** Psychopharmacology. 68(2):191-196, 1980.

Agonistic, locomotor, and stereotyped behavior were measured in male Swiss-Webster mice treated with d-amphetamine (2, 4, or 8mg/kg i.p.) and confronted in their home cages with an intruder mouse. Administration of d-amphetamine to the resident mice decreased the frequency of attacks on the untreated intruder, increased the resident's locomotor activity, and induced a small amount of stereotyped behavior. No tolerance to the antiaggressive effects of d-amphetamine was seen in mice treated chronically with 8 or 16mg/kg/day. However, chronically treated mice showed sensitization to the effects of d-amphetamine on stereotypy and diminished sensitivity to the drug's effect on locomotor activity. No cross-tolerance or cross-sensitization to cocaine was observed. 28 references. (Author abstract modified)

**003326** Oei, Tian Po Sumantri. University of Newcastle (Australia) **Catecholamine depletion by 6-hydroxydopamine and aversive learning: central and peripheral studies. (Ph.D. dissertation).** Dissertation Abstracts International. 39(12):6178-B, 1979. (Not available from Univ. Microfilms), 1978.

Six experiments were conducted in the rat to evaluate the relationship between central and/or peripheral catecholamine (CA) depletion and plasma corticosterone (11-OHCS), the role of plasma 11-OHCS in acquisition of avoidance responses in centrally and/or peripherally depleted rats, and the contributions of peripheral NA and central CAs on acquisition and maintenance of avoidance responses. Results indicate that while peripheral NA is not necessary to avoidance acquisition, it may be useful for avoidance performance in the early stages of acquisition of instrumental responses in aversive learning. Central CAs were found to be necessary for acquisition; and behavioral deficits in central CA depleted rats were more permanent than those in peripheral NA depleted rats. Extensive whole brain depletion and/or peripheral NA depletion did not play a significant role in release of plasma 11-OHCS; nor did resting and postsessional levels of plasma 11-OHCS play a significant role in aversive learning in central and/or peripheral CA depleted animals. (Journal abstract modified)

**003327** Oishi, Ryozo; Suenaga, Noriko; Hidaka, Tadashi; Fukuda, Takeo. Dept. of Pharmacology, Faculty of Medicine, Kyushu University 60, Fukuoka 812, Japan **The role of alpha-adrenoceptors in the regulation of pentylenetetrazol convulsions in mice.** Journal of Pharmacy and Pharmacology. 31(10):709-710, 1979.

The role of alpha-adrenoceptors in regulating susceptibility to pentylenetetrazol (PTZ) convulsions was examined in male CF1 mice. Phentolamine (10mg/kg) significantly elevated the threshold for PTZ-induced twitch, clonic seizure, and tonic extension. Clonidine (1mg/kg) significantly reduced thresholds for twitch and tonic extension. Susceptibility to PTZ convulsions was also increased by intraventricular administration of 6-hydroxydopamine. Results suggest that susceptibility to PTZ convulsions is regulated by facilitatory alpha-adrenoceptors. 16 references.

**003328** Olgiati, Vincenzo R.; Netti, Carmela; Guidobono, Francesca; Pecile, Antonio. Pecile: Dept. of Pharmacology, School of Medicine, University of Milan, Milan, Italy **The central GABAergic system and control of food intake under different experimental conditions.** Psychopharmacology. 68(2):163-167, 1980.

Intracerebroventricular injections of GABA or the GABA transaminase inhibitor enthanolamine-0-sulphate (EOS) decreased food intake in freely fed female Sprague-Dawley rats. EOS also depressed food intake in food deprived animals. These effects were not antagonized by bicuculline. Muscimol increased food intake in freely fed animals, and this effect was antagonized by bicuculline. Bicuculline itself stimulated feeding in freely fed rats and depressed feeding in deprived animals. Results suggest that GABA neurons are involved in the regulation of feeding behavior and that muscimol binds preferentially to GABA receptors in satiety controlling areas. 13 references. (Author abstract modified)

**003329** Olson, Richard D.; Kastin, Abba J.; Lahoste, Gerald J.; Olson, Gayle A.; Coy, David H. Dept. of Psychology, University of New Orleans, New Orleans, LA 70122 **Possible non-narcotic component to action of opiate peptides on tonic immobility.** Pharmacology Biochemistry and Behavior. 11(6):705-708, 1979.

Chickens were tested in a tonic immobility paradigm after a single intraperitoneal injection of the potent opiate analog, (D-A1a2, F5Phe4)-Met-enkephalin-NH2. An inverted U relationship was obtained, with 100mcg/kg being the most effective in prolonging immobility. This dose was used in subsequent studies involving pretreatment with naloxone or diluent followed by treatment with diluent, (D-A1a2, F5Phe4)-Met-enkepahlin-NH2 (a strong opiate), or (D-Phe4)-Met-enkephalin (a weak opiate). Results indicate that, although naloxone had mixed effects in attenuating the duration of tonic immobility, even the analog with negligible opiate activity reliably potentiated the response. Therefore, a component of the effect of opiate peptides on tonic immobility could be due to a nonnarcotic action. 21 references. (Author abstract)

**003330** Onodera, K.; Kisara, K.; Ogura, Y. Ogura: Dept. of Pharmacology, School of Dentistry, Tohoku University, Seiryo-machi 4-1, Sendai 980, Japan **Effect of 5-hydroxytryptophan on muricide response induced by thiamine deficiency.** Archives Internationales de Pharmacodynamie et de Therapie. 240(2):220-227, 1979.

Intraperitoneal injection of 5-hydroxytryptophan (5-HTP) suppressed the muricide response induced by thiamine deficiency in male Wistar rats. The suppressive effect of 5-HTP on muricide was potentiated by pretreatment with the decarboxylase inhibitor Ro4-4602. In contrast, parachlorophenylalanine increased the incidence of muricidal behavior in thiamine deficient animals. It is suggested that muricidal behavior is under the control of serotonergic neurons in the amygdala region. 11 references. (Author abstract modified)

**003331** Osborne, Guy L.; Caul, William F.; Fernandez, Kathleen. Dept. of Psychology, Vanderbilt University, Nashville, TN 37240 **Behavioral effects of prenatal ethanol exposure and dif-**

**ferential early experience in rats.** Pharmacology Biochemistry and Behavior. 12(3):393-401, 1980.

Offspring of rats that were intubated with ethanol during Days 10 through 14 of gestation and offspring in two control groups were compared on measures of growth, viability, and performance in behavioral tasks. Influences of postnatal environment were assessed by using fostering/cross fostering procedures and by providing different postweaning housing conditions. Results indicate that offspring from dams treated with ethanol displayed prenatal and postnatal growth deficiency as well as increased postnatal mortality. In the open field, offspring in the ethanol group were more active than those in the other two groups. Ethanol offspring were also more active in the Y maze and made more avoidance responses and correct discriminations. Early experience as manipulated by the fostering/cross fostering procedures and postweaning rearing conditions had no impact on the effects of prenatal ethanol on offspring growth, viability, or behavior. 32 references. (Author abstract modified)

**003332** Ostrowski, Nancy L.; Foley, Teri L.; Lind, Marcia D.; Reid, Larry D. Reid: Dept. of Psychology, Rensselaer Polytechnic Institute, Troy, NY 12181 **Naloxone reduces fluid intake: effects of water and food deprivation.** Pharmacology Biochemistry and Behavior. 12(3):431-435, 1980.

The mechanism of the naloxone-induced reduction of fluid intake in rats was investigated in water and food deprived animals. Food and fluid deprived and nondeprived male rats showed 36% and 46% decreases, respectively, in sucrose consumption 15 min after injection with 2mg/kg of naloxone in one hr tests. The magnitude of the decrease was not correlated with an index of naloxone's ability to produce a sickness, as measured by the conditioned taste aversion test. Tests with animals scheduled to drink water in a 15 min daily session showed naloxone had similar effects in reducing water intake in 23 hr and 47 hr water deprived rats. Morphine, when self-administered, produced an increase in water intake during 6 hr sessions. The data support the idea that naloxone disrupts a component of normal regulation of ingestion. 16 references. (Author abstract modified)

**003333** Ostrowski, Nancy L.; Stapleton, June M.; Noble, Ralph G.; Reid, Larry D. Psychobiology Program, Psychology Dept., University of Pittsburgh, Pittsburgh, PA 15260 **Morphine and naloxone's effects on sexual behavior of the female golden hamster.** Pharmacology Biochemistry and Behavior. 11(6):673-681, 1979.

The effects of morphine and naloxone on the sexual behavior of the female golden hamster were observed. Large doses of morphine, 80mg/kg, consistently produced sedation and behavioral depression of responses to nociceptive stimuli. Smaller doses of morphine (e.g., 10mg/kg), that produced few other behavioral changes, suppressed a measure of female sexual responding. The suppressive effects on sexual behavior were reversed by 4mg/kg of naloxone. Morphine administered intracerebroventricularly had little effect on sexual responding, even at doses which produced other side-effects. Doses of 4 and 8 mg/kg of naloxone in opioid naive Ss did not reliabley alter sexual responding up to 2 hours after administration. These observations lead to the suggestion that morphine produces effects which are incompatible with full sexual functioning in female hamsters. 41 references. (Author abstract modified)

**003334** Overstreet, D. H.; Russell, R. W.; Helps, S. C.; Messenger, M. School of Biological Sciences, Flinders University of South Australia, Bedford Park, South Australia 5042 **Selective breeding for sensitivity to the anticholinesterase DFP.** Psychopharmacology. 65(1):15-20, 1979.

The hypothesis that genetic factors are involved in sensitivity of physiological and behavioral variables in rats to the irreversible anticholinesterase, diisopropyl fluorophosphate (DFP), was tested. Regression analyses confirm that the selective breeding procedure was successful in establishing a line with increased sensitivity to DFP, but that it failed to produce a line more resistant than the original population. Analyses of variance of the results for the F6, F7, and F8 generations reveal that the sensitive line was more sensitive than either the randomly bred line or the resistant line, while the latter two groups were not significantly different from each other. Biochemical studies indicate that the genetic differences in sensitivity to DFP were not related to differences in cholinesterase or acetylcholinesterase activity. 20 references. (Author abstract modified)

**003335** Palfai, Tibor; Walsh, Thomas J. Psychology Dept., Syracuse University, Syracuse, NY 13210 **Comparison of the long-term cumulative effects of reserpine and syrosingopine on general activity.** Pharmacology Biochemistry and Behavior. 11(5):585-587, 1979.

The question of whether reserpine or its peripherally active analogue, syrosingopine, would produce cumulative effects on general activity following chronic administration was studied. The behavioral consequences of reserpine had previously been shown to include tremors, decreased spontaneous locomotor activity, reduced food intake, and impaired memory formation, possibly due to the drug's effect on biogenic amines mediating these behavioral phenomena. When administered once every 10 days for a total of eight drug treatments, reserpine, but not syrosingopine, produced a cumulative decrease in general motor activity in mice. The maximum depression of activity was evident following the second reserpine administration. Following a 30 day drug free period, animals previously treated with reserpine still exhibited decreased motor activity. The data suggest that chronic reserpine treatment may result in long-term and perhaps permanent, behavioral effects. 20 references. (Author abstract modified)

**003336** Panksepp, Jaak; Meeker, Rick; Bean, N. Jay. Dept. of Psychology, Bowling Green State University, Bowling Green, OH 43403 **The neurochemical control of crying.** Pharmacology Biochemistry and Behavior. 12(3):437-443, 1980.

The capacity of 18 drugs, including those which modify brain opioid, serotonin (5-HT), norepinephrine (NE), dopamine (DA), and acetylcholine (ACh) activity, to modulate separation-induced distress vocalization (DV) in young chicks were studied. Intraperitoneal morphine injections were very effective in reducing DVs and naloxone was found to increase DVs. Smaller bidirectional effects were also observed after pharmacological manipulation of cholinergic and serotonergic systems. Blockade of these systems with atropine and methysergide increased DVs while a facilitation of activity in these systems with pilocarpine and quipazine reduced DVs. Small reductions of DVs could also be achieved with neuroleptics such as haloperidol and chlorpromazine, and with apomorphine, suggesting that reduction of brain dopamine activity reduces DVs, while clonidine was very powerful in reducing DVs, perhaps through autoreceptor reduction of brain NE activity. Chlordiazepoxide was capable of reducing DVs, while imipramine and pentobarbital were essentially without effect. Opiate effects could be obtained as readily following intraventricular as following peripheral drug administration, while cholinergic and serotonergic agents were most effective by the peripheral route. In general, it is concluded that the opiate system had the most powerful specific effect on DV of all systems studied. 25 references. (Author abstract)

**003337** Parisi, Thomas. University of Rochester **The ontogeny of modfication of the acoustic startle reflex in normal rats and in rats treated systemically with 6-hydroxydopamine. (Ph.D. dissertation).** Dissertation Abstracts International. 41(1):401-B, 1980. Ann Arbor, Univ. Microfilms No. 8014338, 137p., 1980.

The development of acoustic starle modification in the normal infant rat and in rats treated systemically with 6-hydroxydopamine (6-OHDA) on days 3, 4, and 5 of postnatal life was investigated. The first five experiments deal with the development of modification of acoustic startle in the untreated neonate by brief auditory, visual, and tactile prestimuli. The later experiments examine the development of modification using auditory and visual prestimuli in animals treated with 6-OHDA. In addition, data describing growth, the first appearance of the startle response, and eyelid opening are presented for both normal and 6-OHDA treated animals, as well as animals pretreated with desipramine. (Journal abstract modified)

**003338** Parrott, R. F.; Batt, R. A. L. ARC Institute of Animal Physiology, Babraham, Cambridge, England **The feeding response of obese mice (genotype, ob ob) and their wild-type littermates to cholecystokinin (pancreozymin).** Physiology & Behavior. 24(4):751-753, 1980.

The feeding response of genetically obese mice that had been reared on a restricted diet and their wild type littermates to cholecystokinin (CCK) (Pancreozymin) were investigated. Following 23 hours food deprivation, Ss were given i.p. injection of either 0, 15, 30, 60, or 120 units/kg CCK in saline vehicle and, 10 minutes later, a series of behavioral tests. Consummatory feeding, drinking, and exploratory activity were recorded for a period of 20 minutes. While 15 units/kg had no effect, higher doses of CCK caused a greater reduction in the feeding rates of obese than in wild type mice. Frequencies of drinking and exploration remained unchanged. Results suggest that the characteristic hyperphagia of obese mice may be due, in part, to low levels of endogenous satiety hormones. 10 references. (Author abstract modified)

**003339** Patel, J. B.; Ciofalo, V. B.; Iorio, L. C. Dept. of Pharmacology, Schering Corporation, Bloomfield, NJ **Benzodiazepine blockade of passive-avoidance task in mice: a state-dependent phenomenon.** Psychopharmacology. 61(1):25-28, 1979.

Four benzodiazepines (diazepam, chlordiazepoxide, halazepam, lorazepam) were tested for their effects on the acquisition of a passive avoidance task in mice. Each of these benzodiazepines, at doses that did not alter overt behavior, blocked acquisition of the passive-avoidance response when they were administered to mice prior to the training session, but not when they were administered after the training session or prior to testing 24 hours later. The block of avoidance responding was reversed, however, when the drugs were administered prior to both training and test sessions. These results suggest that state-dependent learning occurred; i.e., apparent amnesia occurred in the test session with untreated mice that had undergone passive-avoidance learning 24 hours earlier under the influence of drug. 17 references. (Author abstract modified)

**003340** Patel, J. B.; Malick, J. B. Biomedical Research Dept., Stuart Pharmaceuticals, Division of ICI Americas Inc., Wilmington, DE 19897 **Effects of isoproterenol and chlordiazepoxide on drinking and conflict behaviors in rats.** Pharmacology Biochemistry and Behavior. 12(5):819-921, 1980.

The effects of isoproterenol and chlordiazeopoxide on water consumption were studied in a conflict procedure in which thirsty male Wistar rats were punished periodically for licking a water tube. Both drugs induced drinking in water satiated rats and showed significant anticonflict activity in the shock-induced suppression of drinking test. It is suggested that procedures that do not involve primary drives should be used to confirm anxiolytic activity discovered in those that use food or water as reinforcers. 11 references. (Author abstract modified)

**003341** Pavel, S. Institute of Endocrinology, Bucharest, Rumania **Pineal vasotocin and sleep: involvement of serotonin containing neurons.** Brain Research Bulletin. 4(6):731-734, 1979.

The role of serotonergic neurons was explored in relation to the phenomenon that extremely small amounts of arginine vasotocin (AVT) injected into the third ventricle of unanesthetized cats induce non-REM sleep and suppress REM sleep. The same amount of intraventricularly injected AVT increased, at 15 and 30 minutes, 5-hydroxytryptamine (5-HT) and decreased, at 30 and 60 minutes, 5-hydroxyindoleacetic acid (5-HIAA) levels of the brain. Fluoxetine, a specific 5-HT uptake inhibitor, greatly enhanced the non-REM sleep induced by AVT. Neither arginine vasopressin, nor oxytocin was able to affect indole levels of the brain or to enhance non-REM sleep and to suppress REM sleep after fluoxetine, demonstrating the high specificity of AVT effects. Methergoline, a selective central 5-HT receptor blocker, completely prevented AVT induction of non-REM sleep. Extremely small amounts of AVT, which in some cats were unable to induce non-REM sleep and to suppress REM sleep, become effective after pretreatment with small amounts of 5-hydroxytryptophan. It is suggested that AVT induces non-REM sleep and suppresses REM sleep by interfering with 5-HT release at postsynaptic receptor sites. Results strongly support the monoaminergic theory of sleep providing the first evidence that a peptide synthesized by the brain induces sleep by a serotoninergic mechanism. 22 references. (Author abstract modified)

**003342** Petitjean, Francoise; Buda, Colette; Janin, Michele; David, Marcel; Jouvet, Michel. Dept. de Medecine experimentale, Universite Claude-Bernard, 8 avenue Rockefeller, F-69373 Lyon Cedex 2, France **/The effects of chloramphenicol on sleep in the cat: comparison with thiamphenicol, erythromycine, and oxytetracycline./** Effets du chloramphenicol sur le sommeil du chat: comparaison avec le thiamphenicol, l'erythromycine et l'oxytetracycline. Psychopharmacology. 66(2):147-153, 1979.

The effects of various antibiotics, which inhibit protein synthesis, were studied on the sleep/waking cycle of cats. Chloramphenicol (CAP) selectively inhibited paradoxical sleep (SP). Erythromycine induced only a small decrease in SP, while thiamphenicol and oxytetracycline were ineffective. When CAP was injected after thiamphenicol, the SP inhibition was longer than after CAP alone. Combining erythromycine and CAP produced the same effect as one or other of the antibiotics alone, depending only on the interval between administration of the two drugs. Slow wave sleep was decreased only with high doses of CAP and was unaffected by the other three antibiotics. These results suggest that CAP may inhibit a peptide or protein synthesis involved in the mechanisms of SP. 28 references. (Author abstract)

**003343** Petty, F.; Sherman, A. D. Neurochemical Research Laboratories, Dept. of Psychiatry, College of Medicine, University of Iowa, 500 Newton Road, Iowa City, IA 52242 **Regional aspects of the prevention of learned helplessness by desipramine.** Life Sciences. 26(17):1447-1452, 1980.

The effects of desipramine injection into nine discrete brain regions were investigated via the learned helplessness paradigm in rats. Desipramine injected directly into the hippocampus, frontal neocortex, or lateral geniculate body prevented the development of learned helplessness in rats. It did not have this protective effect when injected into the septum, entorhinal cortex, posterior neorcortex, nucleus candatus, nucleus accum-

bens, or amygdala. Neocortical levels of 5-hydroxyindoleacetic acid were significantly higher in rats receiving desipramine in the three behaviorally active areas than in the six other areas or in saline injected control Ss. 22 references. (Author abstract modified)

**003344** Phillips, A. G.; Mora, F.; Rolls, E. T. Rolls: Dept. of Experimental Psychology, University of Oxford, South Parks Road, Oxford OX13UD, England **Intracranial self-stimulation in orbitofrontal cortex and caudate nucleus of rhesus monkey: effects of apomorphine, pimozide, and spiroperidol.** Psychopharmacology. 62(1):79-82, 1979.

The effects of apomorphine, pimozide, and spiroperidol on intracranial self-stimulation (ICSS) in the orbitofrontal cortex and caudate nucleus of the rhesus monkey were investigated, and parallels were drawn of the effects of the drugs on rats. ICSS was significantly attenuated following peripheral injections of spiroperidol at both sites, while pimozide significantly reduced ICSS in the orbitofrontal cortex but not in the caudate nucleus. Licking for a reward was unaffected. Apomorphine had a differential effect on ICSS, attenuating it in the orbitofrontal cortex and facilitating it in the caudate. Apomorphine had no effect on licking for reward. The parallels between the effects of dopamine agonists and antagonists on ICSS in the monkey and rat suggest that dopamine influences self-stimulation of some sites in both species. 19 references. (Author abstract modified)

**003345** Pisa, Michele; Sanberg, Paul R.; Fibiger, Hans C. Division of Neurological Sciences, Dept. of Psychiatry, University of British Columbia, Vancouver, British Columbia V6T 1W5, Canada **Locomotor activity, exploration and spatial alternation learning in rats with striatal injections of kainic acid.** Physiology & Behavior. 24(1):11-19, 1980.

Bilateral injections of kainic acid into the male Wistar rat striatum produced a set of behavioral changes including temporary aphagia and adipsia, abnormal gait, acute and chronically recurrent seizures, and impaired performance of instrumental spatial alternation. In addition to a severe loss of striatal neurons in all kainate treated rats, a loss of extrastriatal neurons was often observed, most consistently involving the pyramidal neurons of the hippocampus. Similar behavioral changes were found in kainate treated rats with combined striatal and hippocampal lesions and in those with no detectable hippocampal damage. Results suggest that striatal degeneration accounted for most of the behavioral impairment. 55 references. (Author abstract modified)

**003346** Poling, A. D.; White, F. J.; Appel, J. B. Behavioral Pharmacology Laboratory, Dept. of Psychology, University of South Carolina, Columbia, SC 29208 **Discriminative stimulus properties of phencyclidine.** Neuropharmacology. 18(5):459-463, 1979.

In a study of the discriminative stimulus properties of phencyclidine (PCP), male albino rats were first trained to discriminate PCP (4.0mg/kg i.p.) from saline in a two lever drug discriminatin task and then tested with two doses of a variety of other drugs. Apomorphine, d-amphetamine, lysergic acid diethylamide, quipazine, atropine, diazepam, and ditran failed to produce responding on the PCP appropriate lever at he doses tested. A 15mg/kg dose did not. Haloperidol, cyproheptadine, physostigmine, and mecamylamine pretreatments did not significantly alter response to PCP and did not themselves produce PCP appropriate responding. Results confirm previous studies suggesting that PCP has unique effects and a wide variety of neurochemical actions. 21 references. (Author abstract modified)

**003347** Poling, Alan; Krafft, Kathy; Chapman, Linda. Dept. of Psychology, Western Michigan University, Kalamazoo, MI 49008 **d-Amphetamine, operant history, and variable-interval performance.** Pharmacology Biochemistry and Behavior. 12(4):559-562, 1980.

The effects of d-amphetamine on the bar-pressing of rats maintained under a variable-interval schedule of water reinforcement were examined as a function of the operant history of the Ss. One group of rats initially received 51 sessions of exposure to a fixed-ratio 20 schedule, while a second group received equivalent exposure to an interresponse time greater than 12 sec schedule. Mean group response rate when stable was over ten times as high under the fixed-ratio schedule as under the interresponse time greater than 12 sec schedule. Response rates of the two groups largely converged across 47 sessions of exposure to a variable-interval 60 sec schedule, at which time response rates for both groups appeared stable. Acute administrations of d-amphetamine sulfate similarly affected mean response rates of both groups: a 0.25 mg/kg dose did not obviously affect rate, while doses of 0.5, 1.0, and 2.0mg/kg produced dose dependent rate decreases. These results indicate that the efficacy of operant history as a determinant of drug effects may be limited to circumstances where current contingencies do not exercise powerful and direct control over behavior. 26 references. (Author abstract)

**003348** Poulos, Constantine X.; Cappell, Howard. Addiction Research Foundation, 33 Russell Street, Toronto, Ontario M5S 2S1, Canada **An associative analysis of pretreatment effects in gustatory conditioning by amphetamine.** Psychopharmacology. 64(2):201-207, 1979.

Two experiments were undertaken in the rat to examine associative interference hypotheses of pharmacological pretreatment effects in conditioned taste aversion. In experiment 1, nonreinforced presentations of drug administration cues completely reversed the attenuating effects of amphetamine pretretament on gustatory conditioning by amphetamine. This finding was replicated and extended in the second experiment, which was also designed to eliminate an alternative nonassociative explanation of these results. Results of experiment 2 demonstrated that, independently of drug pretreatment, ostensibly minor cues (i.e., handling cues) present during flavor conditioning sessions attenuated gustatory aversion. Thus, assoicative blocking must be considered in evaluating existing experiments designed to test the hypothesis that the pretreatment effect is a reflection of pharmacologic tolerance. While it is possible to explanin the present findings exclusively in terms of associative factors, further research needed to clarify a possible role of associated associative manipulation of tolerance. 20 references. (Author abstract modified)

**003349** Pradhan, S. N.; Bhattacharyya, Alok K.; Aulakh, C. S.; Pradhan, Sikta; Bailey, Paul T. Dept. of Pharmacology, College of Medicine, Howard University, Washington, DC 20059 **Cannabis and brain-stimulation reward.** In: Nahas, G., Marihuana: biological effects. Oxford, Pergamon, 1979. 777 p. (p. 567-583).

The effects of delta9-tetrahydrocannabinol (THC) on self-stimulation (SS) behavior in rats were studied, via implanted electrodes at the posterior hypothalamus or area ventralis tegmentum. Its effects were also studied with respect to spontaneous motor activity (SMA), rectal temperature, barbiturate sleeping time, development of tolerance, and brain neurotransmitter levels. Two patterns of THC effects were observed in these experiments. In one type, a gradual drug-induced depression persisted for a prolonged period. The other type, a triphasic effect was characterized by an initial depression followed by a stimulation and then again depression, and was observed in SS in aroused subjects and SMA. The neurochemical studies demonstrated an initial increase in dopamine (DA) in the caudate nu-

cleus and diencephalon/midbrain (DM) and increase in serotonin (5-HT) in DM and pons medulla, followed by increase in DA and decrease in 5-HT and then their reversal in respective brain areas. Development of tolerance to the behavioral depressant effect in SS on repeated administration of THC in SS and lack of cross-tolerance to mescaline were also observed. 28 references. (Author abstract modified)

**003350** Quadagno, D. M.; Hough, J. C.; Ochs, R. L.; Renner, K. J.; Bast, J. D. Bast: Dept. of Anatomy, 415 R. L. Smith Research Center, University of Kansas Medical Center, Kansas City, KS 66103 **Intrahypothalamic actinomycin-D: sexual behavior and nucleolar ultrastructure in the steroid-primed ovariectomized rat and the intact cyclic rat.** Physiology & Behavior. 24(1):169-172, 1980.

The effects of actinomycin-D (Act-D) on sexual behavior and nucleolar ultrastructure were studied in Sprague-Dawley rats after unilateral injections into the medial preoptic area. Steroid-induced sexual preceptivity was inhibited by the nucleolar segregation induced by Act-D. High levels of sexual receptivity were observed when the nucleoli of preoptic cells returned to normal. 6 references. (Author abstract modified)

**003351** Ramirez, Oscar A.; Carrer, Hugo F.; Nasello, Antonia G. Departamento de Farmacologia, Facultad de Ciencias Quimicas, Universidad Nacional de Cordoba, Estafeta 32, 5000 Cordoba, Argentina **Prenatal amphetamine exposure: ovulation, sexual behavior and hypothalamic monoamine content in rats.** Pharmacology Biochemistry and Behavior. 11(6):605-609, 1979.

The effects of prenatal amphetamine exposure on the ovulation, sexual behavior and hypothalamic monoamine content of female offspring of rats injected with amphetamine were investigated. It was found that offspring of amphetamine treated rats have greater sensitivity to estrogen and estrogen/progesterone for the induction of sexual receptivity. Serotonin content in medial hypothalamus of estrogen/progesterone treated rats was decreased with respect to controls. On the other hand, the content of 5-hydroxyindoleacetic acid (5-HIAA) was not different; noradrenaline levels in hypothalamus were also normal. Sex cycle duration and ovulatory phenomena were not affected. 20 references. (Author abstract modified)

**003352** Rastogi, Ram B.; Singhal, Radhey L.; Lapierre, Yvon D. Singhal: Dept. of Pharmacology, School of Medicine, University of Ottawa, 275 Nicholas Street, Ottawa, Ontario K1N 9A9, Canada **Effects of rubidium and cesium on central catecholamines and locomotor behavior in rats.** Journal of Neurochemistry. 34(6):1764-1767, 1980.

The effects of rubidium (Rb) and Cesium (Cs) on the disposition and metabolism of norepinephrine (NE) and dopamine (DA) in rat brain and on locomotor behavior were investigated. Injection of Rb for 4 days tended to elevate locomotor activity; however, the changes became statistically significant only when treatment with this alkali metal ion was continued for a period of 10 days. No change in behavioral activity of rats treated with Cs for 4 or 10 days was noted. Data indicate the Rb treatment not only enhances the synthesis and turnover of NE, but also blocks its reuptake. Chronic treatment with Cs failed to increase DA release in brain and associated locomotor activity in rats. In view of the prolonged half-life (50 days) of Rb in plasma and CSF of man, as well as its inherent toxicity, it remains speculative whether this alkali metal cation will eventually prove useful in the treatment of depressive illness or other mental disorders in humans. 23 references.

**003353** Rauschenberger, Joan Ellen. University of California, Riverside **Role of area postrema in learned taste aversion: a comparison of several drugs. (Ph.D. dissertation).** Dissertation Abstracts International. 40(11):5454-B, 1980. Ann Arbor, Univ. Microfilms No. 8010465, 136p., 1979.

The role of area postrema (AP) in learned taste aversion was assessed by comparing the degree of learned aversion to a variety of drugs in rats with lesions of the AP with aversion in control groups. Ingestion of a novel flavor, sucrose, was paired with injection of either CuS04, LiCl, apomorphine, methylscopolamine, scopolamine, or amphetamine. When CuS04 was the USC, more than one physiological system was involved in the mediation of learned aversions. With high doses of LiC1 or apomorphine, learned aversions were produced in AP lesioned rats. AP lesions prevented formation of conditioned aversions with methylscopolamine and scopolamine. With higher doses of amphetamine, AP lesions did not affect the degree of aversion learning. In many cases, manipulation of the drug dose and route of administration was critical for demonstration of the involvement of multiple mediating systems. (Journal abstract modified)

**003354** Rebec, George V.; Segal, David S. Dept. of Psychology, Indiana University, Bloomington, IN 47401 **Enhanced responsiveness to intraventricular infusion of amphetamine following its repeated systemic administration.** Psychopharmacology. 62(1):101-102, 1979.

Previous findings that long-term administration of d-amphetamine produces a progressive augmentation of behavior were investigated in rats. Ss receiving repeated systemic injections responded to an intraventricular infusion of d-amphetamine with an augmented increase in locomotor activity. These results indicate that central mechanisms, rather than peripheral dispositional factors, subserve the enhanced behavioral response to repeated amphetamine administration. 8 references. (Author abstract)

**003355** Rice, Deborah C.; Gilbert, Steven G.; Willes, Robert F. Toxicology Research Div., Health Protection Br., Bureau of Chemical Safety, Health and Welfare Canada, Ottawa, Ontario K1A OL2, Canada **Neonatal low-level lead exposure in monkeys: locomotor activity, schedule-controlled behavior, and the effects of amphetamine.** Toxicology and Applied Pharmacology. 51(3):503-513, 1979.

Activity levels in monkeys exposed from birth to low levels of lead were assessed. Monkeys were dosed orally with 500micrograms/kg/day lead as lead acetate from Day 1 of life. No overt signs of lead toxicity were observed. At 2 to 3 years of age locomotor activity and performance on a multiple fixed-interval 8 min timeout schedule of reinforcement were studied. Treated monkeys behaved differently from controls during initial sessions, with exposure to lead resulting in increased response rates, decreased median interresponse times, and more responding in the timeout period. Subtle differences in the pattern of responding in the fixed-interval persisted throughout the course of the study. There were no differences in locomotor activity between control and treated pairs of monkeys. It is reported also that there were no differential effects of delta-amphetamine between treated and control monkeys on either locomotor activity or schedule controlled behavior. 43 references. (Author abstract modified)

**003356** Richardson, Daniel Leo. Loyola University of Chicago **Stress, neurotransmitters and avoidance acquisition. (Ph.D. dissertation).** Dissertation Abstracts International. 40(11):5229-B, 1980. Ann Arbor, Univ. Microfilms No. 8011020, 158p., 1980.

The roles of brain serotonergic (5-HT), noradrenergic (NE), cholinergic (ACh), and GABAergic pathways in mediating avoidance learning and response to stress were examined in mice. Different strains of mice were subjected to different stres-

sors (foot shock and social isolation) and sensory deprivation (glossopharyngealectomy, olfactory bulbectomy, and enucleation), and the effects of these stressors and types of sensory deprivation on brain NE, 5-HT, ACh, and GABA concentrations and turnover rates were studied. The effects of stress and a variety of pharmacological treatments on conditioned avoidance learning were also studied. Results suggest that during stress, catecholaminergic systems are activated, as reflected by increased turnover and decreased concentrations. During stress, cholinergic activity may be decreased, thereby, facilitating consolidation. The serotonergic system may be activated in stressful situations by a negative feedback mechanisms, especially following activation of the pituitary adrenal axis. (Journal abstract modified)

**003357** Ridley, R. M.; Scraggs, P. R.; Baker, H. F. Division of Psychiatry, Clinical Research Centre, Watford Road Harrow, Middlesex HA1 3UJ, England **Modification of the behavioural effects of amphetamine by a GABA agonist in a primate species.** Psychopharmacology. 64(2):197-200, 1979.

The effects of the GABA agonist, muscimol, on locomotion was examined in normal and amphetamine treated marmosets. Acute administration of d-amphetamine resulted in a dose dependent increase in small head movements (checking) and an almost total suppression of purposeful activities and social interaction. It had little effect on locomotion and did not produce stereotyped gnawing. When given alone, muscimol decreased locomotion checking, activity, and social interaction, and induced jerking movements at large doses. In combination with amphetamine, muscimol induced persistent stereotyped gnawing. On the basis of these findings and those of previous studies in rodents, it is suggested that compulsive gnawing results from overactivity in the striatal efferent pathway, while checking is probably mediated by extrastriatal sites. Since the behavioral effects of muscimol resemble those of typical neuroleptics with the exception of the induction of gnawing, it is suggested that muscimol, though sedative, may counteract certain extrapyramidal effects of neuroleptic treatment while facilitating their other effects. 19 references. (Author abstract modified)

**003358** Rieke, Garl K. Dept. of Anatomy, College of Medicine, Texas A & M University, College Station, TX 77843 **Kainic acid lesions of pigeon paleostriatum: a model for study of movement disorders.** Physiology & Behavior. 24(4):683-687, 1980.

The utility of kainic acid (KA) lesions of pigeon paleostriatum as a model for the study of movement disorders in mammals was assessed. It is noted that the paleostriatal complex (PC) of the pigeon and the mammalian basal ganglia are considered to be analagous structures on the basis of neuroanatomical and histochemical observations. To test the analogy on a behavioral basis, small volumes of KA were stereotaxically injected unilaterally into the PC. It was hypothesized that if the PC is the avian analogue of the mammalian basal ganglia, then the behavioral problems following KA injection into the PC should be similar to those seen in mammals after injection of KA into the basal ganglia. KA had pronounced neurotoxic effects, particularly upon the large neurons of the PC. The birds demonstrated behavioral disturbances similar to those induced in mammals. More specifically, these include episodes of rapid rotation toward the side of the injection, involuntary movements, and postural disturbances. The pigeon may therefore serve as another useful experimental model system to assess behavioral and histochemical changes associated with movement disorders. 15 references. (Author abstract modified)

**003359** Rigter, Henk; Rijk, Huub; Crabbe, John C. CNS Pharmacology Dept., Scientific Development Group, Organon, Oss, The Netherlands **Tolerance to ethanol and severity of withdrawal in mice are enhanced by a vasopressin fragment.** European Journal of Pharmacology. 64(1):53-68, 1980.

The vasopressin fragment des-Gly9-(Arg8)-vasopressin dicitrate (DGAVP) altered the course of ethanol tolerance in male Swiss mice. Continuous infusion of DGAVP during a 3 day period of ethanol dependence induction exacerbated withdrawal convulsions on day 4 and enhanced residual tolerance on day 5. These effects did not appear to be due to subconvulsive activity of DGAVP or to changes in blood levels of ethanol. 23 references. (Author abstract modified)

**003360** Riley, Edward P.; Lochry, Elizabeth A.; Shapiro, Neil R. Dept. of Psychology, SUNY at Albany, Albany, NY 12222 **Lack of response inhibition in rats prenatally exposed to alcohol.** Psychopharmacology. 62(1):47-52, 1979.

Offspring of mothers who consumed either 32, 19, 8 or 0% of their daily caloric intake in the form of ethanol during pregnancy were tested for passive avoidance. At 8 days, the number of trials to criterion and the within group variability were direct functions of the amount of ethanol consumed by the mother. At 41 to 53 days, the Ss still required more trials to criterion than controls and had faster speeds into the shock compartment of trial 1. A linear dose response function was also evident when the progeny of mothers consuming different doses during pregnancy were compared for conditioned taste aversion. The results indicate that the effect of alcohol exposure in utero are manifested in behavioral outcomes involving response inhibition that are not correlated with the more familiar physical symptoms. 25 references. (Author abstract modified)

**003361** Risner, Marc E.; Jones, B. E. National Institute on Drug Abuse, Division of Research, Addiction Research Center, Lexington, KY **The effects of psychomotor stimulants on single-spatial alternation behavior in dogs.** Psychopharmacology. 63(2):137-141, 1979.

The effects of psychomotor stimulants on dog task performance were investigated. Dogs were trained to pedal press for drinking water in a noncued, single spatial alternation task. After the dogs were exhibiting stable performance at criteria levels, they were given drugs either methylphenidate, d-amphetamine, or phenmetrazine. In general, all four drugs produced similar changes in performance. The number of correct responses was an especially sensitive indicator of drug effects. All four dogs also produced significant increases in both the average response latency and total session duration. 11 references. (Author abstract modified)

**003362** Roberts, D. C. S.; Koob, G. F.; Klonoff, P.; Fibiger, H. C. Dept. of Psychology, Carleton University, Ottawa, Canada K1S 5B6 **Extinction and recovery of cocaine self-administration following 6-hydroxydopamine lesions of the nucleus accumbens.** Pharmacology Bicchemistry and Behavior. 12(5):781-787, 1980.

The injection of 6-hydroxydopamine (6-OHDA) into the nucleus accumbens disrupted cocaine self-administration behavior in male Wistar rats, but this effect did not resemble extinction. Self-administration behavior returned to normal in many animals, and the rate of recovery was correlated with the level of dopamine remaining in the nucleus accumbens. When rats were given methylimipramine or pargyline prior to 6-OHDA to make more extensive and selective lesions, several animals displayed behavior resembling extinction. Apomorphine self-administration was not affected by 6-OHDA treatment. Results suggest that nonstriatal dopamine may subserve cocaine reward. 20 references. (Author abstract modified)

**003363** Roberts, D. C. S.; McCaughran, J. A., Jr.; Fibiger, H. C. A. V. Davis Center for Behavioral Neurobiology, Salk Insti-

tute, P.O. Box 1809, San Diego, CA 92112 **Behavioural effects of 6-hydroxydopamine-induced depletion of spinal noradrenaline.** Canadian Journal of Physiology and Pharmacology. 57(11):1223-1228, 1979.

The behavioral effects of 6-hydroxydopamine (6-OHDA)-induced depletion of spinal noradrenaline (NA) were examined in the rat. Bilateral injection of 6-OHDA into the caudal medulla reduced spinal NA to 6% of control values. No significant NA depletion was found in the hippocampus, cortex, or cerebellum; a small loss of NA was observed in the hypothalamus. Lesions were found to significantly elevate threshold shock levels necessary to elicit jump responses and also abolished the reflexive alternating motor movements produced by decapitation. Data support the hypothesis that spinal NA mechanisms modulate reflexive motor movements. However, no significant effect of these lesions was found on either spontaneous or amphetamine-induced locomotor activity, suggesting that spinal NA does not play a significant role in these behaviors. 43 references. (Author abstract modified)

**003364** Roberts, David Charles Stephen. University of British Columbia (Canada) **On the role of catecholamines in the reinforcing and punishing properties of stimulants and opiates. (Ph.D. dissertation).** Dissertation Abstracts International. 39(12):5868-B, 1979. (Not available from Univ. Microfilms), 1978.

The role of catecholamines in the reinforcing and punishing properties of some opiates and stimulant drugs was examined in rats. 6-hydroxydopamine (6-OHDA) lesions of the n. accumbens produced a marked disruption in cocaine, but not apomorphine, self-administration which in most cases returned to baseline levels after 1 to 3 weeks. Animals with the severest depletion of dopamine (DA) failed to show recovery of cocaine intake. Injections of 6-OHDA aimed at the dorsal and ventral noradrenergic (NA) bundles, despite causing nearly total depletion of forebrain NA, did not significantly affect the rate or pattern of cocaine self-administration. In another series of experiments, 6-OHDA induced depletion of central DA and NA, and severely attenuated an amphetamine-induced conditioned taste aversion (CTA); this attenuation was not the result of a general learning deficit. Selective depletion of hippocampal and cortical NA through intracerebral infusion had no effect on amphetamine-induced CTA. Depletion of forebrain NA attenuated CTA induced by morphine; however, heroin self-administration was not affected by depletion of forebrain NA following 6-OHDA lesions. Pimozide produced an apparent blockade of cocaine reinforcement but had no effect on heroin self-administration. (Journal abstract modified)

**003365** Robertson, R. T.; Majka, J. A.; Peter, C. P.; Bokelman, D. L. Merck Institute for Therapeutic Research, West Point, PA 19486 **Effects of prenatal exposure to chlorpromazine on postnatal development and behavior of rats.** Toxicology and Applied Pharmacology. 53(3):541-549, 1980.

The effects of prenatal exposure to chlorpromazine on postnatal development and behavior of rats were investigated. Chlorpromazine was administered to pregnant rats at doses of 1, 3, or 9mg/kg/day from days 6 to 15 of gestation. The growth, morphologic and reflex development, and reproductive performance of the offspring were recorded. Selected males from all groups were tested in the postweaning period for rotorod performance and activity in an open field. At sexual maturity, selected pups of both sexes were necropsied; mean organ weights were recorded; and histomorphologic and morphometric examinations were performed on coronal sections of the brain of high dose and control males. There was no prenatal evidence of a teratogenic effect. The growth, physical, and reflex development of F1 pups was unaffected during the preweaning period. Postweaning growth of female offspring in all dosage groups was comparable to that of the controls. At 3 and 9mg/kg/day there was a very slight but statistically significant decrease in average bodyweight gain of males in the postweaning period, but the biological significance of this effect is uncertain. Mating performance of offspring exposed prenatally to chlorpromazine was unaffected. In the postweaning period, there were significant increases in activity in an open field and decreases in latency time in male offspring from 3 and 9mg/kg/day dosage groups compared to pooled controls. There were no changes in organ weights and the results of histomorphologic and morphometric examination in brain sections from control and 9mg/kg/day males were comparable. 25 references. (Author abstract modified)

**003366** Robin, Marc M.; Palfreyman, Michael G.; Zraika, Monique M.; Schechter, Paul J. Centre de Recherche Merrell International, 16 rue d'Ankara, F-67084 Strasbourg Cedex, France **An analysis of the cortical and striatal involvement in dyskinesia induced in rats by intracerebral injection of GABA-transaminase inhibitors and picrotoxin.** European Journal of Pharmacology. 62(4):319-327, 1980.

Topical application of the GABA transaminase inhibitors gamma-acetylenic GABA and gamma-vinyl GABA to the cortical surface overlying the striatum produced dyskinesia in male Sprague-Dawley rats. No evidence of drug diffusion to the striatum was obtained. The cortically-induced movements could be duplicated by picrotoxin application to a defined cortical area. Results indicate that this dyskinetic syndrome (characterized by contralateral limb myoclonus) may be cortically induced and not dependent on the interruption of GABA function in the striatum. 24 references. (Author abstract modified)

**003367** Rockman, G. E.; Amit, Z.; Carr, G.; Brown, Z. W.; Ogren, S. O. Center for Research on Drug Dependence, Dept. of Psychology, Concordia University, Montreal, Quebec, Canada **Attenuation of ethanol intake by 5-hydroxytryptamine uptake blockade in laboratory rats: I. Involvement of brain 5-hydroxytryptamine in the mediation of the positive reinforcing properties of ethanol.** Archives Internationales de Pharmacodynamie et de Therapie. 241(2):245-259, 1979.

The role of 5-hydroxytryptamine (5-HT) uptake blockade in the mediation of the positive reinforcing properties of ethanol was investigated in male Wistar rats. Treatment with zimelidine, a 5-HT uptake inhibitor, specifically attenuated ethanol consumption. Rats that preferred ethanol were treated with zimelidine and given ethanol as their only source of fluid; ethanol consumption was reduced when these animals were subsequently given a free choice between ethanol and water. Results suggest that 5-HT mechanisms may be involved in the mediation of the positive reinforcing properties of ethanol. 39 references. (Author abstract modified)

**003368** Rockman, G. E.; Amit, Z.; Carr, G.; Ogren, S.-O. Center for Research on Drug Dependence, Dept. of Psychology, Concordia University, Montreal, Quebec, Canada **Attenuation of ethanol intake by 5-hydroxytryptamine uptake blockade in laboratory rats: II. Possible interaction with brain norepinephrine.** Archives Internationales de Pharmacodynamie et de Therapie. 241(2):260-265, 1979.

Ethanol preferring male Wistar rats were injected with the norepinephrine (NE) reuptake blocker desmethylimipramine (DMI) or vehicle prior to treatment with zimelidine, a 5-hydroxytryptamine (5-HT) uptake inhibitor. The animals pretreated with DMI consumed significantly more ethanol than rats treated with zimelidine alone. Results suggest that the attenuation of ethanol consumption seen after zimelidine treatment

may be due in part to a 5-HT-induced functional depletion of NE. 11 references. (Author abstract modified)

**003369** Rodgers, R. J.; File, Sandra E. School of Psychology, University of Bradford, Bradford, England **Exploratory behaviour and aversive thresholds following intra-amygdaloid application of opiates in rats.** Pharmacology Biochemistry and Behavior. 11(5):505-511, 1979.

To investigate the possible behavioral significance of the amygdaloid opiate system, the effects of intraamygdaloid opiate injections on two behavioral tests were assessed. These tests were response to a novel environment (hole board test) and reactivity to electric shock (flinch/jump test). Microinjections of morphine at either the central or medial nucleus of the amygdala significantly elevated the threshold of response in the flinch/jump test; but only at medial sites did naloxone antagonize this effect. However, in the hold board test, an opposite pattern of results emerged. It is concluded that: 1) the presence or absence of naloxone sensitive opiate receptors cannot always be deduced on the basis of a single behavioral test, and 2) within the amygdaloid complex, two distinct naloxone sensitive opiate systems appear to be involved in the modulation of behavioral responses to different forms of stimulaton. 36 references. (Author abstract modified)

**003370** Rodgers, R. John; Deacon, Robert M. J. Post-Graduate School of Psychology, University of Bradford, Bradford BD7 1DP, England **Effect of naloxone on the behaviour of rats exposed to a novel environment.** Psychopharmacology. 65(1):103-105, 1979.

The hypothesis that endogenous opiates may play a general role in stress responding was tested by administering naloxone hydrochloride to rats exposed to an open field situation. Naloxone treatment produced a decrease in locomotor activity and rearing, and an increase in defecation. A simple dose response relationship was not observed, with the most potent effects exerted by the 1 mg/kg dose. Nevertheless, the results indicate that naloxone increases emotionality in the rat and suggest that opioid peptides may be released under conditions of nonpainful stress. 19 references. (Author abstract)

**003371** Rowland, Neil; Marques, David M.; Fisher, Alan E. Dept. of Psychology, University of Pittsburgh, Pittsburgh, PA 15260 **Comparison of the effects of brain dopamine-depleting lesions upon oral behaviors elicited by tail pinch and electrical brain stimulation.** Physiology & Behavior. 24(2):273-281, 1980.

Male Sprague-Dawley rats with extensive depletion of brain dopamine (DA) after two intraventricular (i.v.t.) injections of 200mcg 6-hydroxydopamine (6-OHDA) showed relatively normal food directed responses to tail pinch (TP) and to electrical stimulation of the lateral hypothalamus. However, rats with similar brain DA depletions induced by single i.v.t. injections of 250mcg 6-OHDA showed a permanent abolition of electrically elicited eating and a chronic reduction in TP-induced behavior. Spontaneous and pinch elicited oral behaviors were absent in rats after intranigral 6-OHDA treatment, which depleted DA by 90% in the nucleus accumbens and almost completely in the striatum. 31 references. (Author abstract modified)

**003372** Sahgal, Arjun; Iversen, Susan D.; Lewis, Michael E.; Trimnell, Laura E. MRC Neuroendocrinology Unit, Newcastle General Hospital, Westgate Road, Newcastle-upon-Tyne, NE4 6BE, England **Effects of ACTH4-10 on a conflict schedule in pigeons.** Communications in Psychopharmacology. 3(4):211-216, 1979.

A multiple conflict schedule in which responding during punishment and nonpunishment was equalized by suitable (FI and FI/pun) reinforcement parameters is described, and the use of the schedule to test the effects of ACTH4-10 and sodium amylobarbitone in pigeons is discussed. The latter drug released responding (i.e., had anxiolytic effects), whereas the former had no consistent effect on performance. Although drug effects depend on the interaction of a large number of variables, it is concluded that the proposed anxiogenic properties of ACTH4-10 cannot be demonstrated on this conflict schedule. 23 references. (Author abstract modified)

**003373** Sahgal, Arjun; Iversen, Susan D. MRC Neuroendocrinology Unit, Newcastle General Hospital, Westgate Road, Newcastle-upon-Tyne NE4 6BE, England **Recognition memory, chlordiazepoxide and rhesus monkeys: some problems and results.** Behavioural Brain Research. 1(3):227-243, 1980.

The effects of chlordiazepoxide (CDP) on recognition memory performance of rhesus monkeys were investigated. Monkeys were taught a variation of the Konorski pair comparison tasks, with and without delay. Once they had learned a discrimination task, delays in stimulus presentation which required memory of a stimulus for from 0 to 16 sec were added, and reliable forgetting curves were obtained. Few impairments of this behavior were observed even after high (80mg/kg, i.p.) doses of CDP. This result is in contrast to previously reported findings with pigeons. CDP failed to disrupt percent correct performance on the tasks although response latencies showed an increase, leading in some cases to a failure to respond within the allocated time. 37 references. (Author abstract modified)

**003374** Saito, Hiroshi; Tsuchiya, Moriyoshi; **Naka, Shinichi**; Takagi, Keijiro. Dept. of Chemical Pharmacology, Faculty of Pharmaceutical Sciences, University of Tokyo, Bunkyo-ku, Tokyo 113, Japan **Effects of Panax ginseng root on acquisition of sound discrimination behaviour in rats.** Japanese Journal of Pharmacology. 29(3):319-324, 1979.

The pole climbing and shuttlebox avoidance tests were used to study the effects of intraperitoneal or oral administration of extracts of Panax ginseng root on the acquisition of conditioned avoidance responses (CAR) and sound discrimination behavior (DB) in male Wistar rats. No significant changes in the acquisition of CAR were seen in animals treated with a lipid soluble fraction or the saponin fraction. Intraperitoneal administration of the saponin fraction produced significant acceleration in the acquisition of DB between a 500HZ signal followed by an electric shock and a 1000Hz signal not associated with shock in rats previously trained to avoid the shock. Small doses of the lipid soluble fraction significantly depressed the acquisition of DB. 20 references. (Author abstract modified)

**003375** Samanin, R.; Caccia, S.; Bendotti, C.; Borsini, F.; Borroni, E.; Invernizzi, R.; Pataccini, R.; Mennini, T. Istituto di Ricerche Farmacologiche Mario, Negri, Via Eritrea, 62, I-20157, Milan, Italy **Further studies on the mechanism of serotonin-dependent anorexia in rats.** Psychopharmacology. 68(1):99-104, 1980.

The effects of 4-(3-indolyl-2-ehyl)piperidine, 2-(1-piperazinyl)quinoline (quipazine), and metachlorophenylpiperazine on food intake in female CD-1 rats were correlated with their effects on serotonergic mechanisms in vitro. Results indicate that marked inhibition of serotonin uptake at central synapses is not sufficient to trigger serotonin dependent anorexia in the rat. Increased release or direct stimulation of postsynaptic receptors may be necessary to obtain this effect. 31 references. (Author abstract modified)

**003376** Samanin, Rosario; Mennini, Tiziana; Ferraris, Alessandro; Bendotti, Caterina; Borsini, Franco. Instituto di Ricerche Farmacologiche Mario Negri, Via Eritrea 62, 20157 Milan, Italy

**Repeated treatment with d-fenfluramine or metergoline alters cortex binding on 3H-serotonin and serotonergic sensitivity in rats.** European Journal of Pharmacology. 61(2):203-206, 1980.

The density of H-tritiated 5-Hydroxytryptamine (5-HT) binding sites in rat cortex was reduced by 23% by 28 day treatment with d-fenfluramine, which releases 5-HT and inhibits its uptake, and increased by 31% by treatment with 5-HT antagonist metergoline for 28 days. The anorectic activity of metachlorophenylpiperazine, a central 5-HT agonist, was also decreased by chronic d-fenfluramine and increased by chronic metergoline. Results indicate that chronic treatment with serotonergic drugs can alter 5-HT receptor number and sensitivity. 8 references.

**003377** Sanberg, Paul R.; Fibiger, Hans C. Dept. of Behavioral Biology, Australian National University, Canberra, A.C.T., Australia **Impaired acquisition and retention of a passive avoidance response after chronic ingestion of taurine.** Psychopharmacology. 62(1):97-99, 1979.

Evidence is presented that oral administration of taurine (0.9%) in the drinking water causes impairment of acquisition and, to a lesser extent, retention of a step down passive avoidance task in rats. No effect occurs on spontaneous locomotor activity or habituation measured in photocell activity cases. No differences are observed in either the taurine treated or control Ss in their sensitivity to electric shock. These observations suggest that the administration of oral taurine may have adverse effects on inhibitory or memory functions. (Author abstract modified)

**003378** Sanders, Barbara. Dept. of Psychology, U-20, University of Connecticut, Storrs, CT 06268 **Withdrawal-like signs induced by a single administration of ethanol in mice that differ in ethanol sensitivity.** Psychopharmacology. 68(2):109-113, 1980.

The effects of a hypnotic does of ethanol were studied in mice bred for long (LS) or short (SS) ethanol-induced sleep times. Under control conditions, the SS mice were more active than SL mice and more susceptible to myoclonic but not to clonic seizures. When tested 7 to 9 hours after injection of ethanol LS and SS mice were less active in the open-field and more susceptible to flurothyl-induced clonic convulsions than control mice, but did not differ significantly from each other. LS mice showed a more pronounced hypothermia than SS mice 2 hours after ethanol treatment, and SS mice showed a slight hyperthermia 6 hours after injection that was not observed at any point in the LS mice. 23 references. (Author abstract modified)

**003379** Sanger, D. J. Pharmacology Dept., Pharmaceutical Division, Reckitt and Colman, Dansom Lane, Kingston-upon-Hull, HU8 7DS, England **The effects of caffeine on timing behaviour in rodents: comparisons with chlordiazepoxide.** Psychopharmacology. 68(3):305-309, 1980.

The effects of caffeine and chlordiazepoxide (CDP) on the responding of Wistar rats and Mongolian gerbils on differential reinforcement of low rate (DRL) schedules were compared. CDP increased response rates, decreased reinforcement frequencies, and increased percentages of response bursts in both species. Caffeine increased response rates and decreased reinforcement frequencies, but failed to systemically increase the percentage of response bursts. In gerbils, d-amphetamine also failed to increase the percentages of response bursts. Combinations of caffeine and CDP generally produced additive effects in rats. 17 references. (Author abstract modified)

**003380** Sansone, Mario; Hano, Jozef. Laboratorio di Psicobiologia e Psicofarmacologia, C.N.R., via Reno n. 1, I-00198 Rome, Italy **Enhancement by chlordiazepoxide of the anticholinergic-induced locomotor stimulation in mice.** Psychopharmacology. 64(2):181-184, 1979.

Spontaneous locomotor activity was studied in mice treated with chlordiazepoxide, atropine, and scopolamine, given alone or in combination. Chlordiazepoxide alone increased activity for a short time, while the two anticholinergic drugs produced longer lasting stimulatory effects. Locomotor stimulation was stronger when chlordiazepoxide and antichloinergics were given in combination. These effects are discussed in terms of a possible retarding effect on habituation to the stimuli of a novel environment and the possibility that cholinergic blockade may result in behavioral disinhibition and favor the effects of central adrenergic stimulation. 36 references. (Author abstract modified)

**003381** Santi, Angelo. Dept. of Psychology, Wilfrid Laurier University, Waterloo, Ontario N2L 3C5, Canada **The effects of sodium pentobarbital on matching and oddity performance in pigeons.** Animal Learning & Behavior. 7(2):229-232, 1979.

The effects of sodium pentobarbital on matching and oddity performance in pigeons were examined by employing a higher order conditional discrimination paradigm, in which the line orientation which was superimposed on all of the response keys signaled whether a response to the matching color or a response to the nonmatching color was correct. All pigeons had extensive previous training in this paradigm and were tested at each of three dosage levels: 5, 7.5, and 10mg/kg. For all birds, a clear dose related decrease in accuracy was observed, but the effect was not differential for matching and oddity trials. Accuracy reductions were accompanied by an increase in position preference on both types of trials. The data are compatible with recent claims that physical identity of the sample and correct comparison stimulus need have no special status for pigeons. 15 references. (Author abstract modified)

**003382** Sara, Susan J. New York University Medical Center, Division of Behavioral Neurology, 341 E. 25th St., New York, NY 10010 **Memory retrieval deficits: alleviation by etiracetam, a nootropic drug.** Psychopharmacology. 68(3):235-241, 1980.

Etiracetam, a nootropic drug related to piracetam, facilitated memory retrieval in male Wistar rats when injected 30 minutes prior to retention testing. The drug was active when memory deficits were induced by electroconvulsive shock, undertraining, or long training to test intervals. The drugs effects were demonstrated in a one trial inhibitory avoidance task and a complex multitrial, spatially distributed approach task. 23 references. (Author abstract modified)

**003383** Sara, Susan J.; David-Remacle, Michele; Weyers, Marc; Giurgea, C. Division of Behavioral Neurology, New York University Medical Center, 240 E. 24th Street, New York, NY 10010 **Piracetam facilitates retrieval but does not impair extinction of bar-pressing in rats.** Psychopharmacology. 61(1):71-75, 1979.

The effect of pretest injection of piracetam on retrieval of a spontaneously forgotten task was investigated. Rats were trained on a continuously reinforced bar-press response for water reward. Seven days later they were retested for retention, with or without pretest injection of the nootropic drug, piracetam. Drug treated animals had significantly shorter response latencies than saline treated animals. The results are interpreted as a facilitation of retrieval processes after forgetting. The experiment was extended under extinction conditions and it was found that after three sessions there was a tendency to facilitate extinction when response latency was used as the extinction index. The clinical interest of a drug which facilitates the retrieval aspect of

the memory process without impairment is discussed. 18 references (Author abstract modified)

**003384** Sbordone, Robert J.; Wingard, Joseph A.; Gorelick, David A.; Elliott, Mark L. Neuropsychiatric Institute, University of California, School of Medicine, 760 Westwood Plaza, Los Angeles, CA 90024 **Severe aggression in rats induced by mescaline but not other hallucinogens.** Psychopharmacology. 66(3):275-280, 1979.

To determine whether mescaline's ability to induce pathological aggression in rats is shared by other hallucinogenic drugs or by nonhallucinogenic structural analogues of mescaline, the effects on shock elicited aggression in male Sprague-Dawley rats of three dosage levels of mescaline, LSD, DMT, psilocin, DMPEA, and 5-OHDA were compared. Mescaline treated rats rarely struck each other, but engaged in nearly lethal biting. While LSD, psilocin, and DMT produced some biting, this did not significantly differ from controls and never resulted in injuries. At higher doses, psilocin, DMT, and DMPEA decreased the amount and intensity of fighting. Rats treated with 5-OHDA or LSD did not differ from controls. Results suggest that mescaline's ability to induce pathological aggression in rats exposed to foot shock is not shared by other hallucinogens or nonhallucinogenic mescaline analogues. 39 references. (Author abstract modified)

**003385** Schechter, Martin D. Dept. of Pharmacology, Northeastern Ohio Universities College of Medicine, Rootstown, OH 44272 **Ability of 3-carboxysalsolinol to produce ethanol-like discrimination in rats.** Psychopharmacology. 68(3):277-281, 1980.

Male Sprague-Dawley rats were trained to discriminate ethanol or apomorphine from a nondrug condition and subsequently tested with 3-carboxysalsolinol (3C-SAL). Results showed that 3C-SAL produced drug responses in ethanol trained rats, but produced only a partial drug response in apomorphine trained animals. Results suggest that salsolinol may be responsible for the discriminability of ethanol in rats and that dopaminergic systems may be involved. 29 references. (Author abstract modified)

**003386** Schiorring, E.; Hecht, A. Psychopharmacological Research Laboratory, Sct. Hans Mental Hospital, Dept. E, DK-4000 Roskilde, Denmark **Behavioral effects of low, acute doses of d-amphetamine on the dyadic interaction between mother and infant vervet monkeys (Cercopithecus aethiops) during the first six postnatal months.** Psychopharmacology. 64(2):219-224, 1979.

The behavioral effects of low (.1, .15, and .2mg/kg), acute doses of d-amphetamine on dyadic interaction during the first 6 postnatal months were examined in mother-infant pairs of vervet monkeys (Cercopithecus aethiops). The fundamental parental care behavior pattern was disrupted, and the mother became isolated in a socially withdrawn phase. She did not respond to the calling signals of the infant and showed behavior in which stereotyped self-grooming behavior and or staring into space were predominant. The reactions of the infants to this amphetamine-induced behavior were different in the two experimental pairs. In the first, the infant increased its approach/avoidance movements; in the second, the infant sat very quietly and close in front of the mother. The mother of the first reacted to the increased approaches of the infant with active rejection. In both groups the mothers did not react with the typical ventral/ventral grasping to either infant's sitting close or to the social anxiety signals of the infant. In spite of differences in behavior changes induced by amphetamine, the main conclusion is that the mothers totally lost their normal and biologically significant interest in their infants. 33 references. (Author abstract modified)

**003387** Schiorring, Erik. Psychopharmacological Research Laboratory, Sct. Hans Mental Hospital, DK-4000 Roskilde, Denmark **An open field study of stereotyped locomotor activity in amphetamine-treated rats.** Psychopharmacology. 66(3):281-287, 1979.

The effect of d-amphetamine on the exploratory pattern of male Wistar rats was studied. Amphetamine-induced stereotyped locomotion was shown by analyzing the route of locomotion in an open field. Details of the analysis are given, normal as well as stereotypic features are discerned, and the results are discussed in relation to contemporary views on locomotion and exploration and on the mechanisms of amphetamine effect. It is suggested that the stereotyped locomotion described might be elicited primarily by changes in the brain DA transmitter systems. 55 references. (Author abstract modified)

**003388** Schiorring, Erik; Hecht, Arthur Psychopharmacological Research Laboratory, Dept. E, Sct. Hans Hospital, DK-4000 Roskilde, Denmark **Behavioral effects of low, acute doses of morphine in nontolerant groups of rats in an open-field test.** Psychopharmacology. 64(1):67-71, 1979.

The social behavioral effect of low, acute doses of morphine was examined in nontolerant rat groups in an open-field test. Groups of eight rats were treated with 2, 3.5, or 5mg/kg body weight doses of morphine or a corresponding volume of isotonic saline solution. The formulation of groups, certain other features of social interaction, plus some individual items (i.e., grooming and rearing) were recorded. Morphine induced an increase in the frequency of group formation, mutual biting, and crawling/play/aggression, without disruptions of grooming and rearing behaviors. The total picture of morphine-induced behavior changes at the dose levels used might be characterized as a polyactivation (or a varied stimulation), different from the selective stimulation reported for d-amphetamine. 39 references. (Author abstract modified)

**003389** Schlatter, J.; Battig, K. Swiss Federal Institute of Technology, Dept. of Behavioral Sciences, Turnerstrasse 1, CH-8092 Zurich, Switzerland **Differential effects of nicotine and amphetamine on locomotor activity and maze exploration in two rat lines.** Psychopharmacology. 64(2):155-161, 1979.

Separate groups of two different rat breeding lines, Roman high avoidance (RHA) and Roman low avoidance (RLA) treated with either saline, nicotine (.2mg/kg), or amphetamine (.4mg/kg) were compared for exploratory efficiency and exploratory locomotion by using two different mazes on alternate testing days. The RHA rats generally showed more locomotion but less intermaze transfer than the RLA rats. Nicotine did not alter exploratory efficiency but stimulated exploratory locomotor activity in RHA rats. Amphetamine stimulated locomotor activity in both rat lines, but this stimulation was weaker in comparison with that of nicotine. In contrast to nicotine, amphetamine impaired exploratory efficiency in the RHA rats. Like nicotine, amphetamine did not significantly affect exploratory efficiency in RLA rats. Results demonstrate that, when the two rat lines are compared, there is a dissociation of the two categories of behavior and a further differentiation between nicotine and amphetamine effects. 30 references. (Author abstract)

**003390** Schmidt, William K.; Way, E. Leong. Stine Laboratory, E. I. du Pont de Nemours & Co. Inc., Newark, DE 19711 **Effect of a calcium chelator on morphine tolerance development.** European Journal of Pharmacology. 63(4):243-250, 1980.

The effect of calicum ion chelation on the development of narcotic tolerance was studied in male Sprague-Dawley rats. Results showed that ethyleneglycol-bis-(beta-aminoethyl ether)-N,N'-tetraacetic acid, a calcium specific chelator, enhanced the

development of tolerance to the analgesic effects of morphine. It is suggested that this effect is due to facilitation of adaptive changes of calcium ion disposition related to the neurochemical mechanisms of narcotic tolerance and dependence. 25 references. (Author abstract modified)

**003391** Schulz, Rudiger; Wuster, Michael; Herz, Albert. Dept. of Neuropharmacology, Max-Planck-Institut fur Psychiatrie, Kraepelinstrasse, 2, D-8000 Munich 40, Germany **Interaction of amphetamine and naloxone in feeding behavior in guinea pigs.** European Journal of Pharmacology. 63(4):313-319, 1980.

Chronic naloxone treatment of schedule fed male Hartley guinea-pigs caused an initial anorexia followed by a return to normal food and water intake. The anorexic effects of amphetamine were not altered in animals treated chronically with naloxone. However, guinea-pigs made tolerant to amphetamine were supersensitive to the effects of naloxone on feeding. Since chronic amphetamine exposure results in elevated beta-endorphin levels in the hypothalamus, it is suggested that enhanced endorphinergic activity compensates for the effect of amphetamine on feeding mechanisms. 26 references. (Author abstract modified)

**003392** Scraggs, P. R.; Ridley, R. M. Division of Psychiatry, Clinical Research Centre, Watford Road, Harrow, HA1 3UJ, Middlesex, England **The effect of dopamine and noradrenaline blockade on amphetamine-induced behaviour in the marmoset.** Psychopharmacology. 62(1):41-45, 1979.

Evidence is presented that acute administration of 4mg/kg d-amphetamine in the marmoset results in a large increase in small head movements (checking), an almost total suppression of purposeful activities, social interaction, but little change in the amount of locomotion. Checking behavior is blocked in a dose dependent manner by 0.03 to 0.18mg/kg haloperidol but not by propranolol, aceperone or diazepam, suggesting dopaminergic mediation of this behavior. The loss of activities and social interaction after amphetamine is not antagonized by any of the above drugs. Locomotion is decreased by haloperidol, propranolol, and diazepam in amphetamine treated Ss and by haloperidol and aceperone in normal Ss. 15 references. (Author abstract)

**003393** Sessions, G. Rufus; Meyerhoff, James L.; Kant, G. Jean; Koob, George F. Division of Neuropsychiatry, Walter Reed Army Institute of Research, Walter Reed Army Medical Center, Washington, DC 20012 **Effects of lesions of the ventral medial tegmentum on locomotor activity, biogenic amines and response to amphetamine in rats.** Pharmacology Biochemistry and Behavior. 12(4):603-608, 1980.

The effects of lesions of the ventral medial tegmentum (VMT) on locomotor activity, biogenic amines, and response to amphetamine were investigated in rats. Rats subjected to electrolytic lesions of the VMT showed long lasting increased locomotor activity in the open field compared to sham operated controls. In addition to severe depletion of mesolimbic dopamine, the lesions also caused significant depletions of striatal dopamine, mesolimbic and striatal norepinephrine, and striatal and hippocampal seotonin. Administration of d-amphetamine sulfate produced similar dose response functions for locomotor activity in both VMT lesioned and sham operated rats despite the extensive depletion of dopamine in the VMT lesioned rats. These results suggest that the mesolimbic dopamine pathway is not the sole substrate for amphetamine stimulated locomotor activity. Electrolytic lesions of the VMT interrupt several neurotransmitter pathways which may produce complex and antagonistic effects on behavior. 37 references. (Author abstract modified)

**003394** Shaw, Nigel; Webster, Donald McD. Dept. of Psychology, University of Auckland, Auckland, New Zealand **Disruption of taste aversion learning by pentylenetetrazol.** Psychopharmacology. 66(2):195-198, 1979.

The memory disruption effect of pentylenetetrazol (PTZ) was studied in regard to taste aversion learning in rats. Rats were taught an aversion to a sucrose taste cue (CS) by pairing it with LiCl-induced toxicosis (UCS). The CS/UCS interval was 30 minutes. Animals were injected with PTZ at 0, 15, 25, 28, or 30 minutes after the CS in an attempt to disrupt taste aversion learning. Only animals given PTZ 30 minutes after the CS (simultaneously with the UCS) showed a significant learning deficit. However, learning deficits were also observed in individual animals given PTZ at 15, 25, and 28 minutes. As lithium salts may produce seizures and abnormal electroencephalographic activity, it is suggested that the neurophysiological consequences of PTZ administration may interact with those of LiCl, causing a greater amnesic effect than PTZ by itself. The resulting interference with the memory trace probably affects either the neural engram underlying the CS or the associative bond between the CS and the UCS. Evidence was also found that PTZ could act as a UCS with which to establish a mild taste aversion. 12 references. (Author abstract modified)

**003395** Shearman, G. T.; Lal, H. Dept. of Pharmacology and Toxicology, College of Pharmacy, University of Rhode Island, Kingston, RI 02881 **Generalization and antagonism studies with convulsant, GABAergic and anticonvulsant drugs in rats trained to discriminate pentylenetetrazol from saline.** Neuropharmacology. 19(5):473-479, 1980.

Male hooded Long-Evans rats were trained on a fixed-ratio 10 schedule of food reinforcement to discriminate a subconvulsive dose of pentylenetetrazol from saline. Picrotoxin and strychnine partially generalized to the pentylenetetrazol discriminative stimulus, but bicuculline and gamma-hydroxybutyrate did not. Valproic acid, sodium pentobarbital, and sodium phenobarbital antagonized the pentylenetetrazol discriminative stimulus, but etomidate, gamma-hydroxybutyrate, gamma-acetylenic GABA, gamma-vinyl GABA, trimethadione, ethosuximide, and diphenylhydantoin did not. The drugs that antagonized the pentylenetetrazol stimulus are all anxiolytics, but share no other common pharmacological property. 44 references. (Author abstract modified)

**003396** Shearman, Gary T.; Lal, Harbans; Ursillo, Richard C. Dept. of Pharmacology, University of Rhode Island, Kingston, RI 02881 **Effectiveness of lofexidine in blocking morphine-withdrawal signs in the rat.** Pharmacology Biochemistry and Behavior. 12(4):573-575, 1980.

The effectiveness of lofexidine in blocking morphine withdrawal signs in the rat was evaluated. Discontinuation of chronic morphine infusion in rats resulted in the reliable occurrence of withdrawal body shakes. This sign of narcotic withdrawal was dose dependently reduced by lofexidine and clonidine. As with clonidine, the activity of lofexidine was not prevented by naloxone. In addition, diarrhea induced by naloxone in morphine dependent rats was also prevented by lofexidine or clonidine pretreatment. These data suggest that lofexidine, like clonidine, may reduce the narcotic withdrawal syndrome in humans. 19 references. (Author abstract modified)

**003397** Shimizu, Takao; Koja, Takeshi; Fujisaki, Tadashi; Fukuda, Takeo. Dept. of Pharmacology, Faculty of Medicine, Kagoshima University, Kagoshima 890, Japan **Effects of peripheral electric stimulation on the central 5-hydroxytryptamine turnover and drug-induced head-twitches in mice.** Brain Research. 193(2):594-597, 1980.

Peripheral electrical stimulation (PES) accelerated the rate of whole brain 5-hydroxytryptamine (5-HT) metabolism in male dd

mice. Head twitching induced by 5-methoxy-N,N-dimethyltryptamine was also potentiated by PES. Results suggest that PES causes functional excitation of 5-HT neurons. 13 references.

**003398** Sietnieks, Anni; Meyerson, Bengt J. Meyerson: Dept. of Medical Pharmacology, Box 573, Biomedicum, S-751 23 Uppsala, Sweden **Enhancement by progesterone of lysergic acid diethylamide inhibition of the copulatory response in the female rat.** European Journal of Pharmacology. 63(1):57-64, 1980.

The inhibitory effect of lysergic acid diethylamide (LSD) on the lordosis response in ovariectomized Sprague-Dawley rats was enhanced in a dose dependent fashion by progesterone, but not by estrogen. Progesterone did not alter the effect of LSD on spontaneous behavior in an exploratory situation. Results suggest that progesterone alters monoaminergic mechanisms related to the action of LSD. 25 references. (Author abstract modified)

**003399** Silberman, Edward K.; Vivaldi, Ennio; Garfield, Joseph; McCarley, Robert W.; Hobson, J. Allan. Hobson: 74 Fenwood Road, Boston, MA 02115 **Carbachol triggering of desynchronized sleep phenomena: enhancement via small volume infusions.** Brain Research. 191(1):215-224, 1980.

Factors affecting the behavioral effects of drugs microinjected into the pontine tegmentum were studied in cats. A reduction in the volume of vehicle dramatically enhanced the capacity of the cholinergic agent carbachol to induce desynchronized sleep-like behavior (Dcarb). Dcarb was also enhanced when passive diffusion was substituted for active pumping of a given volume of carbachol solution. Results also suggested that activation of a localized population of cholineroceptive neurons in the pontine reticular formation is a key step in the generation of physiological desynchronized sleep. 23 references. (Author abstract modified)

**003400** Silverman, Peter B.; Ho, Beng T. Texas Research Institute of Mental Sciences, Houston, TX 77030 **The discriminative stimulus properties of 2,5-dimethoxy-4-methylamphetamine (DOM): differentiation from amphetamine.** Psychopharmacology. 68(3):209-215, 1980.

Male Sprague-Dawley rats trained in a two-lever operant procedure to discriminate 1.5mg/kg 2,5-dimethoxy-4-methylamphetamine (DOM) from saline showed generalization from DOM to mescaline or 2,5-dimethoxy-4-ethylamphetamine (DOET) but not to ()-amphetamine or methylphenidate. Both isomers of DOM generalized with racemic DOM but the (-)-isomer was more potent. The DOM stimulus was completely blocked by the serotonin (5-HT) antagonists cinanserin and methysergide, but not by the peripheral 5-HT antagonist xylamidine or the dopamine antagonist haloperidol. Rats trained to discriminate 1.0mg/kg ()-amphetamine from saline generalized from amphetamine to methylphenidate, but not to mescaline, DOET, racemic DOM, or DOM isomers. The amphetamine stimulus was blocked by pretreatment with haloperidol, but not by cinanserin, methysergide, or xylamidine. 34 references. (Author abstract modified)

**003401** Skolnick, P.; Lock, K.-L.; Paugh, B.; Marangos, P.; Windsor, R.; Paul, S. Laboratory of Bioorganic Chemistry, NIAMDD, NIH, Bethesda, MD 20205 **Pharmacologic and behavioral effects of EMD 28422: a novel purine which enhances (3H)diazepam binding to brain benzodiazepine receptors.** Pharmacology Biochemistry and Behavior. 12(5):685-689, 1980.

A novel purine, N6-2-(4-chlorophenyl)-bicyclo(2.2.2)-octyl-(3)-adenosine (EMD-28422), increased the binding of (3H)diazepam to benzodiazepine receptors in vivo within 10 minutes of i.p. administration. The increase in (3H)diazepam binding was due to an increase in the number of benzodiazepine receptors, rather than to altered affinity. EMD-28422 protected mice against pentylenetetrazole and caffeine-induced seizures and potentiated the anticonvulsant action of subeffective doses of diazepam. The compound also significantly increased punished responding in a conflict situation in rats and caused a long lasting decrease in spontaneous motor activity in mice. 20 references. (Author abstract modified)

**003402** Smith, Donald F. Psychopharmacology Research Institute, Aarhus University Institute of Psychiatry, Psychiatric Hospital, DK-8240 Risskov, Denmark **Central and peripheral effects of lithium on conditioned taste aversions in rats.** Psychopharmacology. 68(3):315-317, 1980.

Male Wistar rats were given i.p. injections of 150mmol/l lithium chloride or sodium chloride or intracerebroventricular (i.c.v.) injections of 150mmol/l lithium chloride, sodium chloride, or artificial cerebrospinal fluid (CSF) after drinking saccharin solution. Saccharin intake was subsequently suppressed only in the i.p. lithium group. The concentration of lithium in brain and CSF was much higher after the i.c.v. injection than after i.p. injection, whereas the opposite was true for plasma lithium levels. Results indicate that the conditioned taste aversion induced by lithium is mediated by peripheral drug effects. 17 references. (Author abstract modified)

**003403** Solanto, Mary V.; Hamburg, Martin D. Dept. of Psychiatry, Case Western Reserve University School of Medicine, 2040 Abington Road, Cleveland, OH 44106 **DDC-induced amnesia and norepinephrine: a correlated behavioral-biochemical analysis.** Psychopharmacology. 66(2):167-170, 1979.

The concurrent effects of diethyldithiocarbamic acid (DDC) on retention performance and on central norepinephrine levels were examined. DDC, a dopamine-beta-hydroxylase inhibitor, when injected into rats 30 minutes to 6 hours before training of a passive avoidance task, impaired formation of long-term memory as indicated by performance on a retention task 24 hours later. Performance of the task was at its minimum when injection occurred 2 to 4 hours prior to training; recovery was evident in animals trained 5 or 6 hours after drug treatment. Catecholamine assay of brains of temporally yoked animals showed that norepinephrine depletion followed a time course paralleling that of the amnesia. These findings support the hypothesis that the degree of memory storage, as reflected in performance following training in a passive avoidance task, can be directly correlated with the level of norepinephrine existing at the time of training. 21 references. (Author abstract modified)

**003404** Spear, Norman E.; Smith, Gregory J.; Bryan, Richard G.; Gordon, William C.; Timmons, Robin; Chiszar, David A. Dept. of Psychology, State University of New York at Binghamton, Binghamton, NY 13901 **Contextual influences on the interaction between conflicting memories in the rat.** Animal Learning & Behavior. 8(2):273-281, 1980.

Internal drug-induced stimuli, nonspecific exteroceptive stimuli, and a relatively specific exteroceptive stimulus were investigated as contextual cues in the sequential avoidance training task. Contextual events redundant to the learning, in sequence, of passive and active avoidance were of one type for the former task and of another for the latter. During later testing, these contextual events were found to determine which of these acquired, conflicting dispositions would be manifested in behavior. It is concluded that mutual interference in retention seems subordinate to the influence of the three types of contextual stimuli tested: drug (pentobarbital), compound, and a relatively unitary stimulus. The defining characteristics of a contextual stimulus and the mechanisms through which contextual events control

the manifestation of learned behaviors and alleviation of interference in retention are discussed. 19 references. (Author abstract modified)

**003405** Spyraki, C.; Papadopoulou, Z.; Zis, B.; Varonos, D. Laboratory of Experimental Pharmacology, Medical School, University of Athens, Goudi 609-Athens, Greece **Effects of diazepam-infrasounds combination on locomotor activity and avoidance behaviour of rats.** Pharmacology Biochemistry and Behavior. 12(5):767-771, 1980.

Diazepam decreased spontaneous activity and facilitated retention of a two-way conditioned avoidance response in male Wistar rats in four shuttlebox sessions. These effects were reversed when diazepam was given to rats exposed to an infrasound environment. Brain norepinephrine and dopamine levels were only slightly affected in either situation. 13 references. (Author abstract modified)

**003406** Stoff, David M.; Moja, Egidio A.; Jeffery, Douglas R.; Gillin, J. Christian; Wyatt, Richard Jed. Laboratory of Clinical Psychopharmacology, National Institute of Mental Health, Saint Elizabeths Hospital, Washington, DC 20032 **Tolerance development to a disruptive effect of beta-phenylethylamine (PEA) on a learned behavior in rats.** Psychopharmacology. 66(2):127-131, 1979.

Tolerance development to a disruptive behavioral effect of beta-phenylethylamine (PEA) was investigated in rats. Daily doses of PEA ranging from 8 to 64mg/kg were administered to rats trained to perform a shuttlebox conditioned avoidance response (CAR) at a high, stable rate. The 8mg/kg dose did not influence the CAR, while larger doses produced dose dependent disruptions. With repeated administration, complete tolerance to CAR disruption was acquired by the third injection of 16mg/kg or by the fifth injection of 32mg/kg and maintained over 10 injections. The use of appropriate controls indicated that tolerance was pharmacological and not behavioral. Over the course of 10 injections, tolerance did not develop to CAR disruption caused by 64mg/kg, and this dose of PEA did not elicit tolerance to stereotyped behavior after 21 injections. Thus, it was shown that lower doses of PEA produce tolerance to CAR disruption, but the highest dose does not because of the presence of incompatible response tendencies (stereotypy) interfering with the CAR. 23 references. (Author abstract modified)

**003407** Stone, W. E.; Javid, M. J. Dept. of Physiology, University of Wisconsin Medical School, Madison, WI 53706 **Quantitative evaluation of the actions of anticonvulsants against different chemical convulsants.** Archives Internationales de Pharmacodynamie et de Therapie. 240(1):66-78, 1979.

Anticonvulsants were tested in male Swiss mice for effectiveness against various chemical convulsants. Ethosuximide was very effective against pentylenetetrazol (PTZ), but ineffective against 3-mercaptopropionate (3-MP), which inhibits GABA synthesis. Trimethadione, chlordiazepoxide, and mesuximide were less effective against 3-MP than against PTZ. Profiles for PTZ, bemegride, bicuculline, and picrotoxin differed from that of 3-MP, suggesting that these agents do not induce seizures primarily by blocking GABA mediated inhibition. The profiles of clinically useful anticonvulsants did not resemble that of aminooxyacetic acid, suggesting these drugs do not act primarily on the GABA system. 31 references. (Author abstract modified)

**003408** Stupfel, Maurice; Masse, Helene; Dague, Corinne. Environmental Nuisances Research Group, French National Institute of Health, 44, Chemin de Ronde, F-78110 Le Vesinet, France **Action of psychoactive drugs on sex-related differences in OF1 mice: intraspecific aggressiveness and acute hypoxia survival.** Psychopharmacology. 63(2):103-111, 1979.

The existence of a relationship between the sex-related differences in 51-day-old OF1 mice, regarding male aggressiveness and their sensitivity to an acute hypoxic 50% lethal challenge was investigated. The effects of psychoactive drugs on these sex differences were also explored. The introduction of a previously isolated male to grouped mice decreased survival to the hypoxic challenge more in females than in males. The previously isolated male, which acted as an aggressor with grouped mice, had a higher hypoxic mortality than the mice of the groups under aggression. Clorazepate abolished the sex-related difference in hypoxic survival in groups in the presence of, but not in the absence of, the previously isolated male. Conversely, hypoxyzine and dexamphetamine suppressed the sex-related difference only in the absence of the aggressor. 18 references. (Author abstract modified)

**003409** Swenson, Richard Michael. University of Iowa **Raphe lesion or 5,7-dihydroxytryptamine injection in the superior colliculus when combined with adrenalectomy produces an abnormal grooming behavior in the cat. (Ph.D. dissertation).** Dissertation Abstracts International. 39(12):6179-B, 1979. Ann Arbor, Univ. Microfilms 7912908, 220 p. 1978.

The effects of raphe lesion or 5,7 dihydroxytryptamine (5,7-DHT) injection in the superior colliculus (SC) were examined in normal and adrenolectomized cats. Neither lesion nor injection induced grooming reflexes in the normal cat, but did induce them in adrenolectomized animals. Treatment with 5-HTP, tranylcyromine, or glucocorticoid hormone abolished grooming reflexes; while elevation of cerebral catecholamine levels by dihydroxyphenylalanine had no effect. Pretreatment with methysergide, a putative serotonergic receptor blocker, failed to block behavioral effects of 5-HTP. Methysergide alone produced a dramatic decrease in grooming behavior similar to that seen after 5-HTP. Raphe lesions caused reductions of serotonin in caudate, hypothalamus, SC, and thalamus, whereas 5,7-DHT only reduced serotonin in the SC. Implications are discussed, and a speculative model of neuronal circuitry mediating grooming reflexes is proposed. (Journal abstract modified)

**003410** Taboada, M. E.; Souto, M.: Hawkins, H.; Monti, J. M. Depto. de Farmacologia y Terapeutica, Hospital de Clinicas, Montevideo, Uruguay **The actions of dopaminergic and noradrenergic antagonists on conditioned avoidance responses in intact and 6-hydroxydopamine-treated rats.** Psychopharmacology. 62(1):83-88, 1979.

The actions of various doses of haloperidol, pimozide, clozapine, and phenoxybenzamine were assessed on a conditioned avoidance response (CAR) in control and 6-hydroxydopamine treated rats. Haloperidol proved most potent in disrupting CAR, followed by pimozide, clozapine, and phenoxybenzamine, respectively. Clonidine did not revert avoidance decrements and induced a further CAR decline. Apomorphine produced a partial but significant reversal of the haloperidol and pimozide-induced depression of conditioned responses. The overall results suggest that CAR depends on both dopamine (DA) and norepinephrine (NE) mechanisms. DA seems to be more significant than NE, however, since the CAR was more depressed when receptors depending on the former neurotransmitter were blocked. 27 references. (Author abstract modified)

**003411** Tagashira, Eijiro; Izumi, Tomoko; Yanaura, Saizo. Dept. of Pharmacology, Hoshi College of Pharmacy, Ebara, Shinagawa-ku, Tokyo 142, Japan **Mode of antagonistic action of levallorphan in morphine-dependent rats and assessment of physical dependence liability.** Japanese Journal of Pharmacology. 29(4):623-630, 1979.

The severity of abstinence signs induced by levallorphan was assessed in male Sprague-Dawley rats given morphine (60 to 100mg/kg/day) in food for 1, 3, or 6 weeks. The rate of maximum weight loss following levallorphan (2mg/kg) administration was correlated with the length of time between morphine withdrawal and levallorphan injection, but not with the duration of morphine treatment. In rats given levallorphan injections 0, 5, and 10 hours after morphine withdrawal, the first injection produced a 7% weight loss but the second and third injections produced little weight loss. 14 references. (Author abstract modified)

**003412** Takahashi, Reinaldo N.; Singer, George. Dept. of Psychology, La Trobe University, Bundoora, Australia 3083 **Self-administration of delta9-tetrahydrocannabinol by rats.** Pharmacology Biochemistry and Behavior. 11(6):737-740, 1979.

The dose/response patterns of delta9-tetrahydrocannabinol (delta9-THC) self-injection in naive rats at 80% reduced bodyweight and 100% bodyweight were investigated on a fixed time 1 minute (FT1) food delivery schedule. Results indicate that food deprived animals tested on a FT1 schedule self-injected low doses of delta9-THC at a free feeding situation. These findings suggest that rats without previous history of drug dependence self-administer low doses of delta9-THC and that the interaction between the food deprivation state and the environmental contingencies introduced by a FT1 schedule is a critical variable in the acquisition period. 21 references. (Author abstract modified)

**003413** Tanner, T. Welsh School of Pharmacy, University of Wales Institute of Science and Technology, Cathays Park, Cardiff, CF1 3NU, Wales **GABA-induced locomotor activity in the rat, after bilateral injection into the ventral tegmental area.** Neuropharmacology. 18(5):441-446, 1979.

Bilateral injections of GABA (10 to 100 mcg) into the ventral tegmental area (VT) of male albino rats induced locomotor hyperactivity, which could be antagonized by pretreatment with picrotoxin (4mg/k i.p.). GABA did not alter the concentration of dopamine in the striatal or mesolimbic (nucleus accumbens and olfactory tubercle, NAOT) regions. However, homovanillic acid (HVA) concentrations were elevated in the NAOT 2 hours after GABA injections in rats pretreated with probenecid (200mg/kg i.p.). The GABA analogue beta-(chlorophenyl)-GABA induced sedation following bilateral injection into the VTA; dopamine concentrations increased in the NAOT and HVA concentrations in the NAOT of probenecid treated animals. Picrotoxin did not antagonize the baclofen-induced sedation. 28 references. (Author abstract modified)

**003414** Tapp, Walter N.; Holloway, Frank A. Department of Psychiatry and Behavioral Sciences, University of Oklahoma Health Sciences Center, P. O. Box 26901, Oklahoma City, OK 73190 **Circadian variations in the effect of alpha-methyl-p-tyrosine on avoidance learning.** Psychopharmacology. 63(2):193-194, 1979.

Circadian variations in alpha-methyl-p-tyrosine's (alpha MT) disruption of active avoidance acquisitions were studied in rats. alphaMT administered between 11.0 and 13,00 h. 17.00 and 19.00 h, and 23,00 and 01.00 h impaired learning, but alphaMT administered between 05.00 and 07.00 h did not impair learning. The time of alphaMT ineffectiveness corresponds with the reported circadian peak in brain catecholamines, suggesting that the circadian susceptibility rhythm of alpha MT depends upon circadian fluctuations of brain catecholamines. 7 references. (Author abstract)

**003415** Tarrab-Hazdai, Rebeca; Edery, Habib. Dept. of Chemical Immunology, Weizmann Institute of Science, Rehovot, Israel **Adipsia and aphagia elicited by intracerebroventricular injections of antiacetylcholine receptor antibodies.** Experimental Neurology. 67(3):670-675, 1980.

Immunoglobulins obtained from rabbits immunized with purified nicotinic acetylcholine receptor isolated from the electric fish Torpedo californica were injected every other day into the left or right cerebral ventricle of a second group of rabbits. A reduction in food and water intake was observed within 7 days, and total adipsia and aphagia developed within 25 to 35 days. Severe spastic paralysis of the limbs was also observed in some animals. These disturbances were attributed to central blockade of cholinergic brain receptors. 22 references. (Author abstract modified)

**003416** Taylor, Maxwell. Dept. of Psychology, Concordia University, Montreal, Canada **Dietary modification of amphetamine stereotyped behaviour: the action of tryptophan, methionine, and lysine.** Psychopharmacology. 61(1):81-83, 1979.

Rats fed diets high in tryptophan, methionine, and tryptophan plus methionine or lysine were subsequently injected with 10mg/kg d-amphetamine to investigate behavior. The amount of amphetamine-induced stereotyped behavior observed varied as as a function of the dietary addition, with methionine showing the greatest difference to controls, and lysine the least. Whole brain catecholamine levels and 5-hydroxytryptamine levels also showed amino acid specific changes. It is suggested that this procedure may offer a predictive technique for the identification of potential pathogenic circumstances, such as variations in dietary elements, or situations that might produce abnormally high tryptophan, methionine, or their respective metabolite levels. 11 references. (Author abstract modified)

**003417** Teal, Janice J.; Holtzman, Stephen G. Dept. of Pharmacology, Emory University School of Medicine, Atlanta, GA 30322 **Stimulus effects of morphine in the monkey: quantitative analysis of antagonism.** Pharmacology Biochemistry and Behavior. 12(4):587-593, 1980.

The ability of narcotic antagonists to block the discriminative stimulus effects of 3.0mg/kg of morphine was evaluated quantitatively in the squirrel monkey using a two choice discrete trial avoidance paradigm. The time course and rlative potency of naloxone and naltrexone for antagonizing morphine's stimulus effects in the squirrel monkey were similar to those determined in rats and pigeons. Complete blockade of morphine's effects was attained with 0.03mg/kg of either antagonist when given simultaneously with morphine, but only naltrexone completely blocked the stimulus effects of morphine when the pretreatment interval was extended to 12 and 18 h. A Schild plot derived from the degree of antagonism of graded doses of morphine by graded doses of naltrexone yielded a line with a slope of -0.03 - 0.2 and an apparent pA2 value of 8.25 or -0.2. These rsults demonstrate the feasibility of quantitatively assessing the drug receptor interactions that subserve the discriminative stimulus effects of morphine in the squirrel monkey. 38 references. (Author abstract)

**003418** Thiebot, M. H.; Jobert, A.; Soubrie, P. Unite de Recherche de Neuropsychopharmacologie de l'INSERM, 2, rue d'Alesia, F-75014 Paris, France **/Comparative effects of muscimol and diazepam on behavioral inhibitions induced in the rat by novelty, punishment, and nonreward./** Effets compares du muscimol et du diazepam sur les inhibitions du comportement induites chez le rat par la nouveaute, la punition et le non-renforcement. Psychopharmacology. 61(1):85-89, 1979.

The effects of diazepam and muscimol on food related behavior in rats were investigated. Muscimol failed to enhance food intake in a nonfamiliar situation, to increase the ingestion of an



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unknown food, or to reduce the inhibition of lever-presses for food elicited by the delivery of an electric shock at every eighth press. It also failed to attentuate the inhibitory effects on responding induced by the suppression of the reinforcement during extinction. Constrastingly, diazepam was found to reduce each type of behavioral inhibition. These data lend support to the hypotheses of GABA control of behavioral inhibition and of GABA involvement in the action of benzodiazepines on inhibition induced by novelty, punishment, or nonreward. 20 references. (Author abstract modified)

**003419** Tikal, K. Srobarova 50, 100 36 Prague 10, Czechoslovakia **Inhibited operant behaviour and magnesium increase in rats after isoprenaline.** Activitas Nervosa Superior. 21(1):62-63, 1979.

The role of isoprenaline in the inhibition of operant behavior and in serum magnesium increase was investigated in Wistar rats. Rats previously trained to a stable rate of performance of an operant task were injected (i.p.) with isoprenaline, and killed by decapitation in the 15th, 30th, 60th, and 120th minute following injection. Serum magnesium was estimated by spectrophotometry. The operant behavior of injected rats decreased significantly. Serum concentration of magnesium reached a maximum in the 30th minute following injection, and was at normal level by the 120th minute postinjection. 7 references.

**003420** Tikal, K. Srobarova 50, 100 36 Prague 10, Czechoslovakia **Dihydroergotoxine antagonizes inhibition of operant behaviour after adrenaline and noradrenaline in rats.** Activitas Nervosa Superior. 21(2):63-64, 1979.

To investigate the mechanism by which adrenaline and noradrenaline inhibits operant behavior in rats, the influence of the alpha blocker dihydroergotoxine on the adrenaline (and noradrenaline) produced inhibition was examined. Dihydroergotoxine administration had only a slight effect on operant behavior, but antagonized the depressant effect of the two catecholamines on operant behavior. The greatly reduced effect of noradrenaline relative to adrenaline on operant behavior is noted. 10 references.

**003421** Tikal, K.; Plevova, J.; Hvizdosova, J. Srobarova 50, 100 36 Prague 10, Czechoslovakia **Behavioural effects of cystamine and mexamine in rats.** Activitas Nervosa Superior. 21(1):59-62, 1979.

Spontaneous and operant behaviors of rats were examined following application of systamine and mexamine to compare the time course of CNS effects of these compounds. Both drugs depressed spontaneous and operant behavior of rats, with cystamine having an effect of longer duration than mexamine. The depression of behavior due to cystamine was found to persist long after the disappearance of the maximum radioprotective effect. 12 references.

**003422** Tombaugh, Tom N.; Tombaugh, Jo; Anisman, Hymie. Dept. of Psychology, Carleton University, Ottawa, Ontario, Canada **Effects of dopamine receptor blockade on alimentary behaviors: home cage food consumption, magazine training, operant acquisition, and performance.** Psychopharmacology 66(3):219-225, 1979.

The effects of pimozide on rat behavior were studied. Administration of pimozide disrupted the initiation, but not the maintenance, of home cage food comsumption. Likewise, number of pellets consumed during magazine training was decreased among pimozide treated rats during the first, but not the second day of training. The acquisition of bar-press response for food reinforcement (using a retractable bar) was severely retarded by pimozide; however, such an impairment was not evident if the animals initially received 2 training days in the absence of the drug. Among rats trained to bar-press to asymptote using a nonretractable bar, pimozide reduced the within and between days bar-press rate such that performance was indistinguishable from that of animals placed on extinction in the absence of drug treatment. When transferred from the pimozide treatment to extinction in the absence of drug, the response rate increased to the level observed during the first session of either extinction or pimozide in the continuous reinforcement condition. Results are discussed in terms of sensory motor and reinforcement consequences of dopamine receptor blockade. 10 references. (Author abstract modified)

**003423** Triana, Edgar; Frances, Richard J.; Stokes, Peter E. Frances: 21 Bloomingdale Rd., White Plains, NY 10605 **The relationship between endorphins and alcohol-induced subcortical activity.** American Journal of Psychiatry. 137(4):491-493, 1980.

The relationship between subcortical seizure activity and behavior induced by alcohol and by beta-endorphin was examined with a male monkey. Results support the hypothesis that naloxone temporarily blocks the epileptogenic property of alcohol and indicate a possible endorphin mediated effect. One theory relating to the abuse of alcohol by narcotics addicts may be that alcohol leads to endorphin release. If alcohol ingestion results in beta-endorphin release, this might help elucidate effects such as analgesia, sedation, appetite suppression, and the phenomenon of loss of control over drinking. 7 references.

**003424** Tseng, Liang-Fu; Ostwald, Thomas J.; Loh, Horace H.; Li, Choh Hao. Dept. of Pharmacology, Medical College of Wisconsin, Milwaukee, WI 53233 **Behavioral activities of opioid peptides and morphine sulfate in golden hamsters and rats.** Psychopharmacology. 64(2):215-218, 1979.

The behavioral effects of beta-endorphin, (D-Ala2, D-Leu5)-enkephalin, and morphine were investigated in golden hamsters and in rats. In golden hamsters, beta-endorphin and (D-Ala2, D-Leu5)-enkephalin induced loss of righting reflex, whereas morphine caused no such effect. Both opiate peptides and morphine caused the inhibition of tailflick response and catalepsy in rats. Beta-endorphin was the most potent, followed by (D-Ala2, D-Leu5)-enkephalin, and then by morphine. The catalepsy induced in rats by (D-Ala2, D-Leu5)-enkephalin was different from that induced by beta-endorphin and morphine, in that it produced catalepsy without muscular rigidity. B-endorphin and (D-Ala1, D-Leu5)-enkephalin caused hypothermia in golden hamsters; morphine was less active in altering body temperature. Beta-endorphin caused hypothermia at high doses and hyperthermia at low doses in the rat. These heterogeneous behavioral responses indicate that multiple types of receptors mediate the effects of opiates in the CNS. 12 references. (Author abstract )

**003425** Urca, Gideon; Nahin, Richard L.; Liebeskind, John C. Liebeskind: Dept. of Psychology, UCLA, Los Angeles, CA 90024 **Glutamate-induced analgesia: blockade and potentiation by naloxone.** Brain Research. 192(2):523-530, 1980.

Injection of 0.5mcl L-sodium glutamate (60mM) into the periaqueductal gray matter of male Sprague-Dawley rats resulted in a short lived analgesia in the tail flick assay. A 1mg/kg dose of naloxone attenuated glutamate-induced analgesia when injected 30 minutes but not 5 minutes before testing. Paradoxically, a 10mg/kg dose of naloxone potentiated glutamate analgesia when injected 5 minutes but not 30 minutes prior to testing. The 10mg/kg dose of naloxone also potentiated analgesia induced by a subeffective (12mM) dose of glutamate. Results suggest that glutamate-induced analgesia may be mediated by processes different from those underlying morphine analgesia and that dose related naloxone antagonism should not be a decisive criterion

for assessing endogenous opioid activity. 27 references. (Author abstract modified)

**003426** Usuda, S.; Sano, K.; Maeno, H. Dept. of Pharmacology and Biochemistry, Central Research Laboratories, Yamanouchi Pharmaceutical Col, Ltd., Itabashi-ku, Tokyo 174, Japan **Pharmacological and biochemical studies on a new potential neuroleptic, N-(1-benzyl-3-pyrrolidinyl) 5-chloro-2-methoxy-4-methylamino benzamide (YM-08050).** Archives Internationales de Pharmacodynamie et de Therapie. 241(1):68-78, 1979.

The pharmacological and biochemical properties of N-(1-benzyl-3-pyrrolidinyl)-5-chloro-2-methoxy-4-methylaminobenzamide (YM-08050) were compared with those of haloperidol (HPD) and chlorpromazine (CPZ) in laboratory animals. YM-08050 showed more potent inhibitory effects than HPD or CPZ on stereotypy and emesis induced by apomorphine methamphetamine-induced stereotypy, conditioned avoidance behavior, and open-field behavior. The new drug also showed more potent effects than HPD and CPZ on tritiated dopamine binding and dopamine sensitive adenylate cyclase in the synaptic membrane fractions of canine caudate nucleus. Results suggest that YM-08050 may be a useful antipsychotic drug, with potent central dopaminergic blocking effects and fewer extrapyramidal side-effects than HPD or CPZ. 20 references. (Author abstract mdoified)

**003427** Valzelli, Luigi; Pawlowski, Leszek. Istituto di Ricerche Farmacologiche Eritrea 62, I-20157, Milan, Italy **Effect of p-chlorophenylalanine on avoidance learning of two differentially housed mouse strains.** Neuropsychobiology. 5(3):121-128, 1979.

The effect of p-chlorophenylalanine (PCPA) on the acquisition of avoidance learning and on brain concentrations of 5-hydroxytryptamine, 5-hydroxyindoleacetic acid, and tryptophan of differentially housed male mice of albino Swiss and DBA strains was studied. The results obtained do not support the hypothesis that learning ability varies inversely with the concentration of brain 5-hydroxytryptamine. PCPA can appear as influencing learning ability of different strains of mice differentially housed, depending more on the emotional baseline of the animals than on brain 5-hydroxytryptamine modification. 53 references. (Author abstract)

**003428** Van Harreveld, Anthonie; Cherkin, Arthur; Davis, Joel L. Division of Biology, California Institute of Technology, Pasadena, CA 91125 **Amnestic potency of proline analogs correlates with anti-spreading depression potency.** Pharmacology Biochemistry and Behavior. 12(4):533-541, 1980.

L-proline, its D-enantiomer, six proline analogs including two homologs (L-azetidine-2-carboxylic acid and DL-pipecolic acid), and five other compounds were examined for their effects on spreading depression (SD) and their amnestic and electrophysiological effects. L-proline, L-baikiain, DL-3,4-dehydroproline, and L-4-hydroxyproline all reduced the incidence of SD in the chick retina and proved to be amnestic. D-proline, L-pyroglutamic acid, L-azetidine-2-carboxylic acid, DL-pipecolic acid, L-glutamic acid diethylester, L-isoleucine, and L-norleucine neither depressed SD nor caused retrograde amnesia. L-prolyl-L-proline L-glutamine did not depress SD at low concentrations but had significant amnestic effects. None of the listed compounds induced EEG disturbances. Implications for memory mechanisms are discussed in terms of these results. 42 references. (Author abstract)

**003429** Van Ree, J. M.; Otte, A. P. Rudolf Magnus Institute for Pharmacology, Medical Faculty, University of Utrecht, Vondellaan 6, 3521 GD Utrecht, The Netherlands **Effects of (Des-Tyr1)-gamma-endorphin and alpha-endorphin as compared to haloperidol and amphetamine on nucleus accumbens self-stimulation.** Neuropharmacology. 19(5):429-434, 1980.

Subcutaneous injection of 2.5 or 25mcg of the beta-endorphin fragment (Des-Tyr1)-gamma-endorphin (DTE) attenuated self-stimulation of the nucleus accumbens in male Wistar rats. This effect was observed only at current intensities near the threshold for eliciting behavior. Haloperidol had a similar effect, but also affected the rate of responding at currents associated with maximal performance. Amphetamine enhanced responding at low and high current intensities. Alpha-endorphin did not influence nucleus accumbens self-stimulation. It is suggested that DTE interferes with mesostriatal dopaminergic neuronal systems projecting to the nucleus accumbens, possibly via an action on synaptic membranes. 26 references. (Author abstract modified)

**003430** Vazquez, Francisca; Tellez, Carolina; de la Mora, Pablo; Brust-Carmona, Hector. Departamento de Fisiologia, Div. de Investigacion, Facultad de Medicina, U.N.A.M., Mexico 20, D.F., Mexico **Modification of motor activity, passive avoidance conditioning and evoked potentials by microinjections of picrotoxin in both caudate nuclei in cats.** Pharmacology Biochemistry and Behavior. 11(5):499-503, 1979.

Further evidence was sought for the theory of GABA inhibition of caudate nucleate (CN) activity, which is apparently necessary for passive avoidance conditioning (PAC). In cats, the acquisition session of a PAC response was carried out following the bilateral administration of picrotoxin or saline in the CN. Twenty hours later the animals were placed in the security compartment and remained there for 600 seconds. In the second session, the cats injected with picrotoxin crossed to the other compartment while the subjects injected with saline did not move. In a second series of experiments, evoked potentials (EPs) were recorded in the CN produced by nucleus centralis medialis electrical stimulation. After picrotoxin application the first and second peaks, which could represent EPSPs, increased while the third peak, which could represent IPSPs, decreased. It is concluded that GABAergic intracaudate transmission maintains a lower level of neuronal discharges and probably participates in the maintenance of a PAC but not in its acquisition. 35 references. (Author abstract modified)

**003431** Verberne, A. J. M.; Taylor, D. A.; Fennessy, M. R. Fennessy: Dept. of Pharmacology, University of Melbourne, Parkville, Victoria 3052, Australia **Withdrawal-like behaviour induced by inhibitors of biogenic amine reuptake in rats treated chronically with delta9-tetrahydrocannabinol.** Psychopharmacology. 68(3):261-267, 1980.

The effects of the biogenic amine reuptake inhibitors fluoxetine, clomipramine, and imipramine on male Wistar rats treated chronically with delta9-tetrahydrocannabinol (THC) were examined. THC reduced the rate of body weight gain and had a biphasic effect on activity (hyperactivity followed by depression), and tolerance developed to these effects. All three reuptake inhibitors induced behavioral responses indicative of withdrawal in the THC treated rats. Fluoxetine was the most potent and imipramine the least, which corresponds to the drugs' rank order of potency in inhibiting 5-hydroxytryptamine reuptake. 23 references. (Author abstract modified)

**003432** Waldbillig, Robert J. Dept. of Psychology, University of Florida, Gainesville, FL **Suppressive effects of intraperitoneal and intraventricular injections of nicotine on muricide and shock-induced attack on conspecifics.** Pharmacology Biochemistry and Behavior. 12(4):619-623, 1980.

The suppressive effects of intraperitoneal and intraventricular injections of nicotine on muricide and shock-induced attack on

conspecifics were investigated in rats. It was found that i.p. injections of nicotine suppressed mouse killing in a dose dependent manner. The suppression of mouse killing by nicotine was not blocked by hexamethonium, a peripheral nicotinic receptor blocking agent. Mecamylamine, a nicotinic blocking agent with central effects, did reduce the inhibition of attack produced by nicotine. Both i.p. and intraventricular injections of nicotine suppressed shock-induced attack on conspecifics. Shock elicited flinch, vocalization, and escape were not influenced by nicotine injections. These findings further support the view that muscarinic and nicotinic compounds produce antagonistic effects on certain types of attack behavior. 14 references. (Author abstract modified)

**003433** Wallnau, Larry B. Dept. of Psychology, State University College at Brockport, Brockport, NY 14420 **Tonic immobility in domestic fowl: anticataleptic effects of quipazine.** Pharmacology Biochemistry and Behavior. 12(3):347-352, 1980.

The effects of quipazine, a putative serotonergic agonist, on tonic immobility (TI) elicited in domestic fowl by a brief period of physical restraint were investigated. Quipazine in doses of 5 to 25mg/kg produced marked decreases in TI duration, and quipazine treated animals required more elicitation attempts before displaying TI. Quipazine also blocked the haloperidol enhancement of tonic immobility. In another experiment, quipazine produced stereotyped responses in chickens which yielded increases in activity on a stabilimeter platform. Results are discussed in terms of serotonergic and dopaminergic mechanisms underlying catalepsy. 42 references. (Author abstract modified)

**003434** Walsh, Thomas J.; Palfai, Tibor. Psychology Dept., Syracuse University, Syracuse, NY 13210 **Peripheral catecholamines and memory: characteristics of syrosingopine-induced amnesia.** Pharmacology Biochemistry and Behavior. 11(4):449-452, 1979.

The effect of syrosingopine, a peripherally acting reserpine analogue, on retention of a passive avoidance task was examined in male CD-1 mice. Amnesia was observed 1 week after training in mice treated with 2.5, 4.0, or 6.0mg/kg syrosingopine 2 hours before training, but not in those injected with syrosingopine 24 or 0.5 hours before training or immediately after training. The syrosingopine-induced amnesia was blocked by systemic administration of 0.5 or 0.75mg/kg norepinephrine or 50mg/kg dopamine up to 10 minutes after training. Results suggest that rauwolfia alkaloids such as reserpine and syrosingopine produce amnesia by interfering with catecholamine dependent peripheral memory modulating processes. 22 references. (Author abstract modified)

**003435** Walsh, Thomas J.; Palfai, Tibor. Dept. of Psychology, Syracuse University, Syracuse, NY 13210 **Memory storage impairment or retrieval failure: pharmacologically distinguishable processes.** Pharmacology Biochemistry and Behavior. 11(4):453-456, 1979.

Reserpine and its peripherally acting analogue, syrosingopine, both produced amnesia for a passive avoidance task in male CD-1 mice which was still evident 35 days after training. However, the amnesia induced by syrosingopine could be reversed by repeated exposure to the training apparatus, but the amnesia induced by reserpine could not. The effects of these drugs on memory consolidation and retrieval are discussed. 25 references. (Author abstract modified)

**003436** Watanabe, Kazuhito; Yamamoto, Ikuo; Oguri, Kazuta; Yoshimura, Hidetoshi. Dept. of Hygienic Chemistry, School of Pharmacy, Hokuriku University, Kanazawa 920-11, Japan **Comparison in mice of pharmacological effects of delta8-tetrahydrocannabinol and its metabolites oxidized at 11-position.** European Journal of Pharmacology. 63(1):1-6, 1980.

The pharmacological effects of delta8-tetrahydrocannabinol (delta8-THC) and its metabolites were compared in male ddN mice. Results showed that 11-0H-delta8-THC and 11-oxo-delta8-THC were more potent than delta8-THC in inducing catalepsy and hypothermia and in prolonging pentobarbital sleeping time. These metabolites were also much less toxic than the parent compound. Delta8-THC-11-oic acid was the least active compound tested. 27 references. (Author abstract modified)

**003437** Watanabe, Shigenori; Inoue, Masayoshi; Ueki, Showa. Dept. of Pharmacology, Faculty of Pharmaceutical Sciences, Kyushu University, Fukuoka 812, Japan **Effects of psychotropic drugs injected into the limbic structures on mouse-killing behavior in the rat with olfactory bulb ablations.** Japanese Journal of Pharmacology. 29(3):493-496, 1979.

Muricidal behavior was studied in male Wistar-King-A rats given bilateral olfactory bulb ablations and then injected with psychotropic drugs in various parts of the limbic system. Acetylcholine and serotonin had no effect on muricide. Noradrenaline suppressed muricide in 11 of 16 rats when injected into the medial amygdala. Chlorpromazine, chlordiazepoxide, and diphenhydramine had no significant effect on muricide when injected into any limbic structure, but did suppress muricide when injected systemically. Atropine, imipramine, amitriptyline, and doxepine significantly suppressed muricide, particularly when injected into the medial amygdaloid nucleus. Methamphetamine suppressed muricide when injected into the medial or anterior amygdaloid nucleus, but only at high doses. Results indicate that the amygdala, septum, and hippocampus do not play an important role in the antimuricidal effects of chlorpromazine and chlordiazepoxide. Imipramine, like tricyclic antidepressants, appear to act in the medial amygdaloid nucleus. 12 references.

**003438** Watson, P. J.; Short, Margaret Anne; Huenink, Gary L.; Hartman, David F. Dept. of Psychology, University of Tennessee, Chattanooga, TN 37402 **Diazepam effects on hypothalamically elicited drinking and eating.** Physiology & Behavior. 24(1):39-44, 1980.

The effects of diazepam on eating and drinking elicited by electrical stimulation of the lateral hypothalamus (ESLH) were studied in male Long-Evans rats. Diazepam reduced thresholds for stimulation bound eating but not for drinking. The failure of the tranquilizer to facilitate water intake during stimulation provides evidence against the hypothesis that (ESLH) induces a state of emotionality that blocks the initial display of primary drives evoked by the stimulation. 28 references. (Author abstract modified)

**003439** Wayner, E. A.; Singer, G.; Wayner, M. J.; Barone, F. C. Singer: Dept. of Psychology, LaTrobe University, Bundoora, Victoria 3083, Australia **The effects of several barbiturates on lithium chloride induced taste aversion.** Pharmacology Biochemistry and Behavior. 12(5):803-806, 1980.

A lithium-induced aversion to saccharin in male Wistar rats was attenuated by pentobarbital (9mg/kg), phenobarbital (60mg/kg), or barbital (80mg/kg), but not by amobarbital (30mg/kg) or secobarbital (20mg/kg). Phenobarbital and amobarbital had dipsogenic effects in saline treated controls. A synergistic interaction between lithium chloride and sodium phenobarbital, barbital, and secobarbital was observed. 15 references. (Author abstract modified)

**003440** Wayner, E. A.; Singer, G.; Wayner, M. J.; Barone, F. C. Singer: Dept. of Psychology, LaTrobe University, Bundoora, Victoria 3083, Australia **The taste aversion induction properties**

**of two long duration barbiturates.** Pharmacology Biochemistry and Behavior. 12(5):807-810, 1980.

Phenobarbital (60mg/kg) was more potent than barbital (80mg/kg) in inducing conditioned taste aversion to saccharin in male Wistar rats. The duration of the taste aversion induced by lithium chloride and phenobarbital was longer than that produced by lithium chloride alone or in combination with barbital. Results suggest that the two barbiturates have dissimilar aversive properties. 13 references. (Author abstract modified)

**003441** Wenger, Galen R. Dept. of Pharmacology, Mail slot 521, University of Arkansas for Medical Sciences, 4301 West Markham St., Little Rock, AR 72201 **Effects of clozapine, chlorpromazine and haloperidol on schedule-controlled behavior.** Pharmacology Biochemistry and Behavior. 11(6):661-667, 1979.

The effects of clozapine, chlorpromazine, and haloperidol on responding under a multiple fixed-ratio 30, fixed-interval 600 seconds (FR30/FI600) schedule of food presentation were investigated in mice and pigeons. In both species, low doses were without effect and moderate to high doses of all three antipsychotics decreased responding. In contrast to other behavioral tests used to preduct antipsychotic activity, clozapine was equipotent or more potent than chlorpromazine in decreasing responding under the multiple FR30/FI6000 schedule. The order of potency observed in the mouse was haloperidol greater than chlorpromazine greater than clozapine. The order of potency in the pigeon was haloperidol greater than clozapine greater than chlorpromazine. In mice and pigeons, the rate of responding under the FR component was decreased at lower than, or the same doses of clozapine as that required to decrease FI responding. However, in both species, chlorpromazine and haloperidol decreased FI responding at lower doses or the same dose as that required to decrease FR responding. 22 references. (Author abstract modified)

**003442** Wenger, John Robert. University of Washington **Learned tolerance to depressant drugs. (Ph.D. dissertation).** Dissertation Abstracts International. 40(12):5862-B, 1980. Ann Arbor, Univ. Microfilms No. 8013615, 81p., 1980.

Tolerance to ethanol, sodium pentobarbital, and diazepam is examined via literature review and a series of experiments, and a general theory of tolerance, which posits that tolerance is mediated by learning is presented. Previous reports that tolerance to drugs, especially ethanol, is not mediated by learning are reanalyzed from a learning perspective, and the methodology of these studies is critically evaluated. A series of before/after designs were employed to partition tolerance into components attributable to the effects of intoxicated practice or to drug exposure per se. (Journal abstract modified)

**003443** Wilcox, Richard E.; Riffee, William H.; Smith, Robert V. Dept. of Pharmacology, University of Texas at Austin, Austin, TX 78712 **Pharmacological basis for N-n-prcɔylnorapomorphine induced stereotypic cage climbing and behavioral arousal in mice.** Pharmacology Biochemistry and Behavior. 11(6):653-659, 1979.

Six neurotransmitter receptor blockers (atropine, phentolamine, sotalol, syproheptadine, naloxone, and haloperidol or spiroperidol) were compared in mice for their ability to alter cage climbing and behavorial arousal induced by N-n-propylnorapomorphine (NPA) to evaluate the utility of the NPA induced cage climbing as a model for assessing the dose response and time response effects of potential antiparkinsonian agents. Results indicate the pretreatment with the dopamine blockers haloperidol and spiroperidol, significantly antagonize both response to NPA and shift the cage climb dose response curve to the right 15 fold. In contrast, the muscarinic cholinergic (atropine), alpha noradrenergic (phentolamine), beta noradrenergic (sotalol), serotonergic (cyproheptadine), and opiate (naloxine) receptor blockers uniformly did not attenuate activity due to NPA. These results suggest that cage climbing and arousal induced by aporphines is mediated via dopamine receptor stimulation and that these responses provide useful in vivo models for accurate evaluation of certain classes of dopamine agonists with clinical utility. 20 references. (Author abstract modified)

**003444** Williams, J.; Davies, J. A. Dept. of Pharmacology, Welsh National School of Medicine, Heath Park, Cardiff CF4 4XN, Wales **The action of DL-2,4-diaminobutyric acid on the cataleptogenic effects of pilocarpine and alpha-flupenthixol in rats.** Psychopharmacology. 64(1):81-83, 1979.

Whether the modification of the GABAergic system by the GABA neuronal uptake inhibitor DL-2,4-diaminobutyric acid (DABA) would effect cholinergic (pilocarpine) and/or neuroleptic alpha-flupenthixol (alpha-FPT)-induced catalepsy was examined in the rat. DABA pretreatment was shown to enhance significantly both alpha-FPT and pilocarpine-induced catalepsy. DABA alone had no cataleptic activity. Thus, DABA potentiates the cataleptogenic effects of both these agents. These effects may be attributed to DABA enhancement of GABAergic activity in the strionigral pathway as a direct result of its ability to enhance brain GABA levels by uptake inhibition. Such an enhancement has been proposed (Kim et al, 1971) to have a direct inhibitory effect on the nigrostriatal dopaminergic system resulting in increase inhibition of the system, and hence the observed potentiation of the neuroleptic effect. 14 references (Author abstract modified)

**003445** Winter, J. C. 127 Farber Hall, SUNY, Buffalo, NY 14214 **Effects of the phenethylamine derivatives, BL-3912, fenfluramine, and Sch-12679, in rats trained with LSD as a discriminative stimulus.** Psychopharmacology. 68(2):159-162, 1980.

Six CFN rats were trained to discriminate lysergic acid diethylamide (LSD, 100mcg/kg) from saline and then tested with the phenethylamine derivatives BL-3912, fenfluramine, and Sch-12679. BL-3912 substituted completely for LSD in the two lever choice task, but responding to Sch-12679 and fenfluramine was not fully appropriate for the LSD or saline condition. The LSD-like effects of the drugs were antagonized by pretreatment with BC-105, a serotonergic antagonist that blocks the stimulus effects of indole and phenethylamine hallucinogens. 36 references. (Author abstract modified)

**003446** Witkin, Jeffrey M.; Carter, Richard B.; Dykstra, Linda A. Dept. of Pharmacology, School of Medicine, 231-H University of North Carolina, Chapel Hill, NC 27514 **Discriminative stimulus properties of d-amphetamine-pentobarbital combinations.** Psychopharmacology. 68(3):269-276, 1980.

Male White-Carneaux pigeons were trained to discriminate intramuscular injections of 1.0mg/kg d-amphetamine from water, 5.6mg/kg pentobarbital from water, or 1.0mg/kg d-amphetamine from 5.6mg/kg pentobarbital. In subsequent tests with different doses, the percentage of responses on the drug key was directly related to drug dose. Amphetamine produced a dose related antagonism of the effects of pentobarbital in birds trained to discriminate pentobarbital from water or d-amphetamine. All birds were trained to discriminate a combination of d-amphetamine and pentobarbital from d-amphetamine or pentobarbital alone, indicating the discriminative stimulus properties of the drug combination are different from those of either drug alone. 43 references. (Author abstract modified)

**003447** Woolf, Clifford J.; Mitchell, Duncan; Barrett, Graham D. Dept. of Physiology, Windeyer Building, Middlesex Hospital

Medical School, Cleveland St., London W1P 6DB, England **Antinociceptive effect of peripheral segmental electrical stimulation in the rat.** Pain. 8(2):237-252, 1980.

The flexor withdrawal response to noxious stimuli was diminished in male rats with complete spinal transections. Peripheral electrical stimulation delayed the flexor response in a naloxone reversible manner in spinal rats, but the antinociceptive action of the stimulation was less than that observed in intact rats. Depleion of 5-hydroxytryptamine (5-HT) by systemic pretreatment with parachlorophenylalanine diminished the effect of electrical stimulation and of morphine in intact rats, but not in the spinal animals. Results indicate that peripheral electrical stimulation excites naloxone dependent antinociceptive mechanisms at spinal and supraspinal levels and that the supraspinal mechanism is associated with 5-HT. 43 references. (Author abstract modified)

**003448** Woolverton, William L.; Balster, Robert L. Pharmacology Dept., Medical College of Virginia, Virginia Commonwealth University, Richmond, VA 23298 **Reinforcing properties of some local anesthetics in Rhesus monkeys.** Pharmacology Biochemistry and Behavior. 11(6):669-672, 1979.

Reinforcing properties of several local anesthetics were determined in rhesus monkeys experienced in the intravenous self-injection of cocaine. Intravenous procaine and, occasionally, tetracaine maintained response rates higher than did vehicle injections in most monkeys. In contrast, lidocaine, procainamide, and diethylaminoethanol (a metabolite of procaine) failed to maintain responding resulting in their intravenous delivery. These results demonstrate that not all local anesthetics are positive reinforcers in the rhesus monkey when delivered intravenously. Further, the reinforcing properties of procaine probably cannot be attributed to its metabolite diethylaminoethanol. The data suggest that short acting, esteratic local anesthetics are most likely to have reinforcing properties in the rhesus monkey. 14 references. (Author abstract)

**003449** Woolverton, William L.; Balster, Robert L. Balster: Box 726, Medical College of Virginia Station, Richmond, VA 23298 **Tolerance to the behavioral effects of phencyclidine: the importance of behavioral and pharmacological variables.** Psychopharmacology. 64(1):19-24, 1979.

The effects of phencyclidine (PCP) on the behvior of rats responding to a fixed-interval 1 min schedule were determined before, during, and after a period of daily PCP injections. The effects of acute PCP on overall response rate were biphasic: low doses increased and high doses decreased rates. In addition, PCP produced dose related decreases in quarter life; and high doses of PCP decreased the number of reinforcers delivered. During the daily injection regimen, roughly a twofold tolerance developed to the effects of 8mg/kg PCP on response rate in animals receiving presession or postsession injections of this dose, emphasizing the predominance of pharmacological variables in PCP tolerance. However, slight differences between these groups in tolerance development and in the rate of tolerance loss demonstrated that behavioral variables can influence tolerance to the behavioral effects of PCP. 20 references. (Author abstract)

**003450** Woolverton, William L.; Martin, Billy R.; Balster, Robert L. Dept. of Pharmacology, Medical College of Virginia, Virginia Commonwealth University, Richmond, VA 23298 **Modification of the behavioral effects of phencyclidine by repeated drug exposure and body weight changes.** Pharmacology Biochemistry and Behavior. 12(5):761-766, 1980.

Tolerance to the inhibitory effect of phencyclidine (PCP) on milk intake was observed in male Sprague-Dawley rats treated chronically with PCP or saline. Tolerance in the saline group was attributed to increased body weight. In a second experiment, the acute effects of PCP were found to be reduced in high weight animals, compared to low weight rats. When animals were treated with 3H-PCP, brain 3H-PCP and total radioactivity were significantly lower in the high weight animals than in the low weight animals. 16 references. (Author abstract modified)

**003451** Yamada, Katsushi; Furukawa, Tatsuo. Dept. of Pharmacology, School of Medicine, Fukuoka University, Fukuoka 814, Japan **Dopaminergic inhibition involved in the alpha-naphthoxyacetic acid-induced jumping behavior in mice.** European Journal of Pharmacology. 63(4):321-326, 1980.

Alpha-naphthoxyacetic acid (alpha-NOAA, 250 to 700mg/kg i.p.) elicited a dose dependent jumping behavior in male ddY mice. The drug also induced hypothermia, retching, head shaking, salivation, and lacrimation. The alpha-NOAA-induced jumping behavior was markedly antagonized by apomorphine (1mg/kg), and the effect of apomorphine was in turn inhibited by haloperidol (2mg/kg). Phentolamine, reserpine, disulfiram, tranylcypromine, haloperidol, scopolamine, bicuculline, diazepam, and lithium only partially antagonized the alpha-NOAA-induced jumping. Results indicate that the jumping behavior elicited by alpha-NOAA is due to inhibition of dopaminergic activity. 31 references. (Author abstract modified)

**003452** Yanai, Joseph; Tabakoff, Boris. Dept. of Anatomy and Embryology, Hebrew University, Hadassah Medical School, P. O. Box 1172, Jerusalem, Israel **Altered sensitivity to ethanol following prenatal exposure to barbiturate.** Psychopharmacology. 68(3):301-303, 1980.

Ethanol sensitivity was studied in offspring of female mice fed milled mouse food containing 3g/kg phenobarbital in days 9 through 18 of pregnancy. When tested at 50 days of age, male offspring exposed to phenobarbital prenatally were resistant to the hypnotic effects of ethanol; their ethanol sleep time was 33% shorter than that of controls. Brain ethanol levels upon awakening were higher in offspring of barbiturate treated mothers than in controls. 19 references. (Author abstract modified)

**003453** Yano, Ichiro; Nishino, Hitoo; Murano, Tadashi. Dept. of Physiology, Faculty of Medicine, Toyama Medical and Pharmaceutical University, Toyama 930-01, Japan **Anatgonism by naloxone of tolerance and dependence in mice given a single dose of morphine.** Japanese Journal of Pharmacology. 29(3):357-366, 1979.

The development of morphine analgesia, tolerance, and dependence was studied in male ddY mice given various doses of naloxone at various times after morphine administration. Naloxone antagonized the effects of morphine in a dose and time dependent fashion. The time course of development of tolerance to a single dose of morphine almost paralleled that of morphine dependence, but the time course for the disappearance of tolerance did not coincide with that for the disappearance of dependence. 24 references. (Author abstract modified)

**003454** Young, Gerald A. Dept. of Pharmacology and Toxicology, University of Maryland School of Pharmacy, 636 West Lombard St., Baltimore, MD 21201 **Naloxone enhancement of punishment in the rat.** Life Sciences. 26(21):1787-1792, 1980.

Naloxone enhancement of punishment effects on conditioned responding was investigated in rats. Ss were trained to lever-press on a variable interval 1 minute schedule of reinforcement for food pellets. Subsequently in punishment sessions, lever-presses also produced electric grid shocks on a fixed ratio 20 schedule. With punishment, lever-pressing levels were reduced by about 15%. When naloxone was administered prior to pun-

ishment sessions, shocks reduced lever-pressing levels by about 50% following the 3mg/kg dose and by about 80% following the 10mg/kg dose. This naloxone-induced enhancement of the effect of punishment was probably mediated through an antagonism of naturally occurring brain peptides with opiate-like activities. 29 references. (Author abstract modified)

**003455** Zelger, Jurg L.; Carlini, E. A. Depto. de Psicobiologia, Escola Paulista de Medicina, Rue Botucatu, 862-1 andar, 04023 Sao Paulo, Brazil **Anorexigenic effects of two amines obtained from Catha edulis Forsk. (Khat) in rats.** Pharmacology Biochemistry and Behavior. 12(5):701-705, 1980.

The anorexigenic effects of two amines obtained from Catha edulis Forsk. (Khat) were studied in Wistar rats. Cathine (phenylpropanolamine) and cathionine (alpha-aminopropiophenone) both reduced food intake when given acutely and reduced body weight when given chronically. Cathionine was more effective than cathine, and both were less active than amphetamine. Partial or total cross-tolerance was observed among the three drugs. 28 references. (Author abstract modified)

**003456** Zetler, G. Institut fur Pharmakologie, Medizinische Hochschule Lubeck, D-2400 Lubeck, Germany **Analgesia and ptosis caused by caerulein and cholecystokinin octapeptide (CCK-8).** Neuropharmacology. 19(5):415-422, 1980.

Subcutaneous injection of caerulein and C-terminal octapeptide of cholecystokinin (CCK-8) produced sedation, palpebral ptosis, and analgesia in the hot plate and writing tests (but not the tail flick test) in male NMRI mice. Petagastrin was inactive. Caerulein was more active than CCK-8, and both were more active than morphine. Low doses of naloxone antagonized the analgesic effects, but did not alter ptosis. Morphine tolerance enhanced ptosis, but did not alter the analgesic effects. 43 references. (Author abstract modified)

**003457** Zilberman, Yael; Lichtenberg, Dov; Gutman, Yehuda. Lichtenberg: Dept. of Pharmacology, Hebrew University-Hadassah Medical School, P.O. Box 1172, Jerusalem, Israel **The use of phospholipid liposomes for lithium administration. Polydipsic effect and tissue distribution of lithium.** Journal of Pharmacy and Pharmacology. 31(9):619-621, 1979.

Administration of lithium entrapped in phospholipid liposomes increased lithium-induced polydipsia in male Sabra rats, but did not accelerate the onset of this effect. Compared to standard lithium chloride, the liposome entrapped lithium chloride produced larger accumulations of lithium in the liver, kidney, and spleen, but not in brain. The time course of polydipsia in these animals suggested dependence on intracellular lithium concentrations, but the rate of development appeared to depend on some additional factor. 10 references. (Author abstract modified)

## 05 TOXICOLOGY AND SIDE EFFECTS

**003458** Alexander, G. J.; Lieberman, K. W.; Stokes, P. Dept. of Psychiatry, Cornell University Medical College, 1300 York Ave., New York, NY 10021 **Differential lethality of lithium isotopes in mice.** Biological Psychiatry. 15(3):469-471, 1980.

The effect of administering lithium isotopes in toxic doses of equal sizes to mice was studied. Li-6 proved to be more lethal than the natually occurring mixture of lithium isotopes (Li-N). The possibility that elimination of Li-6 from the lithium compounds used therapeutically might reduce the side-effects experienced by patients is raised. 7 references.

**003459** Ali, S. Fatehyab; Chandra, Om; Hasan, Mahdi. Hasan: Brain Research Center, Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh 202001, India **Effects of an organophosphate (dichlorvos) on open field behavior and locomotor activity: correlation with regional brain monoamine levels.** Psychopharmacology. 68(1):37-42, 1980.

Daily administration of O,O-dimethyl-2:2-dichlorovinyl phosphate (dichlorvos, 3mg/kg i.p.) for 10 days significantly depressed the open-field behavior of male Charles Foster rats. Ambulation, rearing, and defecation were depressed on day 7 but showed various degrees of recovery on day 10. Dopamine was significantly reduced on days 5 and 7 but showed a 13% recovery in the brainstem on day 10. Norepinephrine was significantly reduced in the cerebral hemisphere, and serotonin was decreased in the cerebral hemisphere and brainstem; neither amine showed significant recovery on day 10. 20 references. (Author abstract modified)

**003460** Altura, Burton M.; Weinberg, Julio. Dept. of Physiology, State University of New York Downstate Medical Center, Brooklyn, NY 11203 **Urethane and contraction of vascular smooth muscle.** 67(2):255-263, 1979. British Journal of Pharmacology.

In a concentration as low as 0.001M, urethane inhibited the development of spontaneous mechanical activity in male Wistar rat aortic strips and portal vein segments. Urethane produced a dose dependent attenuation of contractions induced by adrenaline, angiotensin, and potassium chloride. Calcium-induced contractions of potassium depolarized aortae and portal veins were also attenuated by urethane in a dose dependent fashion. All of these inhibitory effects were completely and rapidly reversed when the anesthetic was washed out of the organ baths. A variety of pharmacological antagonists failed to mimic or alter the inhibitory effects of urethane. Results suggest that plasma concentrations of urethane commonly associated with induction of surgical anesthesia can directly induce relaxation of vascular muscle. 32 references. (Author abstract modified)

**003461** Besluau, D.; Gauthier-Rahman, S.; Halpern, B. Institut D'Immuno-Biologie, Hopital Broussais, 96, rue Didot, F-75674 Paris Cedex 14, France **The protective effect of some phenothiazine derivatives against streptolysin O.** British Journal of Pharmacology. 67(2):173-177, 1979.

Subcutaneously administered chlorpromazine (CPZ) and promethazine (PMZ) protected Swiss albino mice and New Zealand black mice against lethal i.v. doses of streptolysin-O. Three other phenothiazine derivatives had similar but less pronounced effects. The protective effect developed slowly, with maximal protection 4 hours after CPZ or PMZ injection. The haemolytic activity of streptolysis-O in vitro was also inhibited by CPZ. 30 references. (Author abstract modified)

**003462** Brown, T. C. K.; Leversha, A. Royal Children's Hospital, Parkville, 3052, Australia **Comparison of the cardiovascular toxicity of three tricyclic antidepressant drugs: imipramine, amitriptyline, doxepin.** Clinical Toxicology. 14(3):253-256, 1979.

The cardiovascular toxicity of three tricyclic antidepressants, imipramine, amitriptyline, and doxepin, was compared. The parameters investigated were the tendency to cause hypotension and the dose required to induce cardiac arrhythmia. Six puppies were observed at weekly intervals using the three drugs in rotation. It was found that imipramine was less toxic than the other two drugs in regard to the dosage levels required to produce cardiac arrhythmias and hypotension. 1 reference. (Author abstract modified)

**003463** Davis, W. Marvin; Borne, Ronald F.; Hackett, Robert B.; Waters, I. W. Dept. of Pharmacology, University of Mississippi School of Pharmacy, University, MS 38677 **Lethal syner-**

**gism of phencyclidine with a precursor and contaminant, 1-piperidinocyclohexanecarbonitrile.** Life Sciences. 26(24):2105-2111, 1980.

The acute median lethal dose (LD50) was determined in rats and mice for phencyclidine (PCP) or 1-piperidinocyclohexanecarbonitrile (PCC) individually and in combination. The LD50 of PCP was 2.3 mg/kg or 2.5 times higher than the LD50 of PCC in mice or rats, respectively. For mice, combinations (8:1 or 4:1) of PCP and PCC showed additive synergism, while in rats a 2:1 combination caused subadditive synergism. Dogs receiving an intravenous infusion of PCP plus PCC (4:1) died at a one third lower dosage of PCP than when PCP was given alone. Prior treatment with sodium nitrite significantly elevated the i.p. LD50's in mice for PCC alone or PCP plus PCC (3:1) as it did for KCN. These data support the inference that toxicity from PCC arises primarily from the cyanide ion which it releases. The possibility of a toxic synergism in the course of human exposure to PCC contaminated abstract)

**003464** Drew, W. G.; Kostas, Jeanne; McFarland, D. J.; De Rossett, Sarah E. Laboratories of Behavioral Neurophysiology, Dept. of Psychiatry, University of Kentucky Medical Center, Lexington, KY 40506 **Effects of neonatal lead exposure on apomorphine-induced aggression and stereotypy in the rat.** Pharmacology. 18(5):257-262, 1979.

Male Long-Evans hooded rats were exposed to lead in maternal milk and tested for apomorphine-induced aggression at 90 days of age. The large increase in aggression in response to 5.0mg/kg apomorphine in control rats was markedly attenuated in lead treated rat pairs. Apomorphine-induced stereotypy was not affected. These results provide a further demonstration of persistent behavioral abnormalities resulting from early exposure to lead at levels which do not affect weight gain or mortality. 30 references. (Author abstract modified)

**003465** End, David W.; Carchman, Richard A.; Ameen, Richard; Dewey, William L. Dept. of Pharmacology, Medical College of Virginia, Richmond, VA 23298 **Inhibition of rat brain mitochondrial calcium transport by chlordecone.** Toxicology and Applied Pharmacology. 51(1):189-196, 1979.

Assessment of radiolabeled calcium ion transport in rat brain mitochondria following in vitro and in vivo exposures to the neurotoxic insecticide chlordecone revealed a locus for chlordecone's mitochondrial impairment in the coupling reactions of oxidative phosphorylation. Mitochondrial transport supported by either succinate (free energy supplied via electron transport) or ATP (free energy supplied via the Mg2ATPase reaction) was inhibited by low concentrations of chlordecone. Administration of a tremorigenic dose of chlordecone to rats similarly inhibited both succinate and ATP supported Ca uptake in brain mitochondria in vitro. Studies on the subcellular distribution of (14C)chlordecone in rat brain following in vivo administrations were compared to those on the mitochondrial uptake of (14C)chlordecone in vitro. Administration of the tremorigenic dose of chlordecone produced mitochondrial chlordecone concentrations which were comparable to the tissue concentrations achieved by exposing mitochondria to chlordecone in vitro. These data lend further support for mitochondrial inhibition as a mechanism for chlordecone toxicity. 24 references. (Author abstract modified)

**003466** Geller, I.; Gause, E.; Kaplan, H.; Hartmann, R. J. Southwest Foundation for Research and Education, P. O. Box 28147, San Antonio, TX 78284 **Effects of acetone, methyl ethyl ketone and methyl isobutyl ketone on a match-to-sample task in the baboon.** Pharmacology Biochemistry and Behavior. 11(4):401-406, 1979.

The effects of acetone, methyl ethyl ketone (MEK) and methyl isobutyl ketone (MIBK) on the performance of juvenile male baboons on a match to sample discrimination task were examined. Animals were exposed to half the threshold limit value for each gas for 7 days. Response times were slowed under acetone, MEK, or MIBK. Exposure to a combination of the same doses of MEK and MIBK produced a consistent increase in extra responses during delay and a concomitant decrease in response times, possibly as a result of changes in tissue uptake and metabolism. 15 references. (Author abstract modified)

**003467** Geller, I.; Hartmann, R. J.; Randle, S. R.; Gause, E. M. Southwest Foundation for Research and Education, P. O. Box 28147, San Antonio, TX 78284 **Effects of acetone and toluene vapors on multiple schedule performance of rats.** Pharmacology Biochemistry and Behavior. 11(4):395-399, 1979.

Male Sprague-Dawley rats trained to press a lever for liquid food reward on a multiple fixed-ratio (FR) fixed-interval (FI) schedule of reinforcement were exposed to 150ppm of acetone or toluene for 0.5, 1, 2, or 4 hours. Acetone produced minimal changes on FR/FI responding with the 0.5 hour exposure, increased FR and FI rates during the 1 hour exposure, decreased FI and FR responses during the 2 hour exposure, and had variable effects during the 4 hour exposure. Rate changes under toluene were qualitatively similar to those induced by acetone: an initial enhancement of FR and FI rates occurred during the shorter exposure periods, followed by a decrease in rates during the longer exposure periods. 26 references. (Author abstract modified)

**003468** Kolber, Alan R.; Krigman, Martin R.; Morell, Pierre. Research Triangle Institute, P. O. Box 12194, Research Triangle Park, NC 27709 **The effect of in vitro and in vivo lead intoxication on monosaccharide transport in isolated rat brain microvessels.** Brain Research. 192(2):513-521, 1980.

Monosaccharide transport was studied in brain microvessels isolated from Long-Evans rats exposed to lead acetate (0.025 to 1.0mg/g/day) from postnatal days 5 to 25. Results revealed a block in facilitated transport of 3-0-methylglucose (30MG), as well as damage to endothelial cells resulting in increased passive permeability. Microvessel preparations from animals treated for only 2 days (prior to sacrifice on postnatal day 7) were more sensitive to lead treatment than those from adults; equivalent lead burden induced a greater increase in passive permeability to 30MG in the younger animals. In microvessels isolated from untreated animals, a concentration of 0.1mcM lead acetate abolished facilitated transport of 30MG in vitro. 18 references. (Author abstract modified)

**003469** Kretzschmar, H.; Kirchner, F.; Takano, K. Takano: Dept. of Physiology, University of Gottingen, Humboldtallee 7, D-3400 Gottingen, Germany **Relations between the effect of tetanus toxin on the neuromuscular transmission and histological functional properties of various muscles of the rat.** Experimental Brain Research. 38(2):181-187, 1980.

Various doses of tetanus toxin were injected into three hindlimb and two forelimb muscles of male Wistar rats. Differences in sensitivity were observed in these five muscles. These differences may reflect differential distribution of endplates with varying structures and sensitivities to this toxin. (Author abstract modified)

**003470** Liebman, Jeffrey; Neale, Robert. Research Dept., Pharmaceuticals Division, Ciba-Geigy Corp., Summit, NJ 07901 **Neuroleptic-induced acute dyskinesias in squirrel monkeys: correlation with propensity to cause extrapyramidal side effects.** Psychopharmacology. 68(1):25-29, 1980.

In squirrel monkeys treated repeatedly with haloperidol at intervals of 7 to 14 days, subsequent acute administration of haloperidol-induced dystonia and dyskinesias. Chlorpromazine, fluphenazine, metoclopramide, tetrabenazine, and Su-23397 also elicited dyskinesias in monkeys primed with haloperidol. Dyskinesias were less marked after thioridazine and were not observed after clozapine, baclofen, or diazepam. The ability of antipsychotic drugs to elicit dyskinesia in haloperidol primed monkeys was correlated with their reported propensity to induce extrapyramidal side-effects in clinical use. 20 references. (Author abstract modified)

**003471** Minchin, M. C. W. Dept. of Physiology, University of Sheffield, Sheffield S10 2TN, England **Veratrum alkaloids as transmitter-releasing agents.** Journal of Neuroscience Methods. 2(2):111-121, 1980.

The neurotransmitter releasing effects of veratrum alkaloids, such as proveratrine, veratridine, and cevadine, are discussed. Various veratrum alkaloids are able to induce the release of a variety of neurotransmitter substances from a number of preparations. The role of calcium in this process is not clearly understood, but it appears that the veratrum-induced release of catecholamines and acetylcholine is calcium dependent, whereas the veratrum-induced release of amino acids is not. The depolarizing veratrum alkaloids may be a valuable tool in dissociating the neuronal and glial origins of released transmitters. 67 references.

**003472** Morgan, J. P.; Mohammed, S.; Van Maanen, E. F. Dept. of Medicine, Mayo Clinic, Rochester, MN 55901 **Sustained hypotension after chronic chlorpromazine treatment in normotensive dogs.** Archives Internationales de Pharmacodynamie et de Therapie. 240(2):228-239, 1979.

The effects of chronic treatment with chlorpromazine hydrochloride (CPZ, 50mg/kg/day) on the cardiovascular and autonomic nervous system of normotensive dogs were examined. Initial mean arterial pressure was 113 Hg in control animals, compared to 81 Hg in dogs given CPZ for 7 days and 84 Hg in those treated for 23 days. Responses to bilateral carotid occlusion, stimulation of the lumbar sympathetic chain, hindlimb flow pressure determinations, and intraarterial injections of norepinephrine indicated that postganglionic adrenergic nerve blockade, probably at the level of the sympathetic nerve ending, was the major cause of the hypotension. Results indicate the CPZ may be useful in the treatment of some psychotic patients who are also hypertensive. 21 references. (Author abstract modified)

**003473** Morgan, Michael E. University of Utah **Short-term and long-term effects of methamphetamine on biogenic amine metabolism in extra-striatal dopaminergic nuclei. (Ph.D. dissertation).** Dissertation Abstracts International. 40(12):5629-B, 1980. Ann Arbor, Univ. Microfilms No. 8012504, 50p., 1980.

The short-term and long-term effects of multiple toxic doses of methamphetamine on catecholaminergic, serotonergic, and cholinergic metabolism in the neostriatum, nucleus accumbens, olfactory tubercle, and median eminence areas of the rat brain were investigated. Methamphetamine (15mg/kg) was administered every 6 hours for five doses, and biogenic amine metabolism was monitored for up to 30 days following treatment. Results suggest that the serotonergic neurons are more sensitive to the toxic effects of methamphetamine than the dopaminergic neurons, whereas the cholinergic neurons seem to be unaffected. (Journal abstract modified)

**003474** Oka, Makoto; Yamada, Kiyoko; Kamei, Chiaki; Yoshida, Kouichi; Shimizu, Masanao. Dept. of Pharmacology, Research Laboratories, Dainippon Pharmaceutical Co., Ltd., Suitashi, Osaka 564, Japan **Differential antagonism of antiavoidance, cataleptic and ptotic effects of neuroleptics by biperiden.** Japanese Journal of Pharmacology. 29(3):435-445, 1979.

The interaction of the anticholinergic agent biperiden with various neuroleptics was examined in the catalepsy, ptosis, and antiavoidance tests in male ddY mice. Biperiden antagonized the cataleptic effects of most neuroleptics to some extent, but had no significant influence on their ptotic effects. Biperidine markedly antagonized the antiavoidance effect of haloperidol, trifluperidol, and perphenazine; moderately antagonized the antiavoidance effect of chlorpromazine; and showed only slight antagonism of the antiavoidance effects of thioridazine, chlorprothixene, levomepromazine, and clozapine. In neuropharmacological tests, haloperidol, trifluoperidol, and perphenazine showed selective antidopaminergic activity, while chlorprothixene, levomepromazine, and clozapine showed antidopaminergic, antiadrenergic, and anticholinergic activities. Results suggest that biperiden antagonism can be used to predict the potency of extrapyramidol side-effects associated with neuroleptic drugs. 35 references. (Author abstract modified)

**003475** Oredipe, O. A.; Stohs, S. J. Dept. of Biomedicinal Chemistry, College of Pharmacy, University of Nebraska Medical Center, Omaha, NE 68105 **Effects of lithium on time to onset of aconitine-induced initial arrhythmia and ventricular tachycardia.** Archives Internationales de Pharmacodynamie et de Therapie. 240(2):249-256, 1979.

The effects of lithium on the time of onset of aconitine-induced initial arrhythmia and ventricular tachycardia were determined in male Swiss-Webster mice. Animals were given lithium chloride in doses of 1.73, 3.0, 5.1, and 8.8mEq/kg/day for 5 days or 8.8mEq/kg/day for 1, 3, 5, 7, and 10 days. Lithium prolonged the time to onset of ventricular tachycardia in a dose and time dependent manner. The lithium pretreatment had no effect on time to onset of aconitine-induced initial arrythmia. The median lethal dose was 15.3mEq/kg. The delayed onset of ventricular tachycardia can be explained in part by the influence of lithium on myocardial cations and catecholamines and by the pharmacological effect of lithium on Purkinje fibers. 21 references. (Author abstract modified)

**003476** Ramsay, Peggy B.; Krigman, Martin R.; Morell, Pierre. Morell: Biological Sciences Research Center, 220H, Division of Health Affairs, University of North Carolina, Chapel Hill, NC 27514 **Developmental studies of the uptake of choline, GABA and dopamine by crude synaptosomal preparations after in vivo or in vitro lead treatment.** Brain Research. 187(2):383-402, 1980.

The kinetics of sodium dependent, high affinity uptake of choline and dopamine by striatal synaptosomes and of GABA by cortical synaptosomes were examined in developing control and lead treated Long-Evans hooded rats. The amount and developmental pattern of neurotransmitter uptake was not markedly altered by chronic lead exposure. In preparations from 20 to 26-day-old rats, in vitro addition of lead resulted in a 20% increase in Vmax for dopamine in the absence of calcium; this stimulation was reduced in the presence of added calcium. Lead slightly inhibited the calcium dependent spontaneous release of dopamine from preloaded synaptosomes and partially substituted for calcium in the potassium evoked release of dopamine and GABA. 54 references. (Author abstract modified)

**003477** Ray, D. E. Toxicology Unit, MRC Laboratories, Woodmasterne Road, Carshalton, Surrey, England **An EEG investigation of decamethrin-induced choreoathetosis in the rat.** Experimental Brain Research. 38(2):221-227, 1980.

EEG and evoked potential recordings from the cerebral cortex and subcortical areas were obtained in rats treated with decamethrin, a neurotoxic pyrethoid insecticide. The motor

symptoms (limb rigidity and choreoathetosis), cortical and subcortical spiking, suppression of cortical evoked responses, and increased caudate neuronal activity in these animals suggested decamethrin acts primarily on the extrapyramidal motor system. Decamethrin-induced extrapyramidal hyperexcitabiity may provide a useful model for studies of extrapyramidal disorders. (Author abstract modified)

**003478** Scivoletto, R.; Lima, F. Bessa; Fortes, Z. B.; Hell, N. S. Instituto de Ciencias, Biomedicas da Universidade de Sao Paulo Caixa Postal 4365, Sao Paulo CEP 05508, Brazil **Effects of dl-tranylcypromine on LD50 of pentobarbital in the rat.** Pharmacology. 19(4):182-184, 1979.

The median lethal dose (LD50) of pentobarbital was determined in female Wistar rats with or without pretreatment with 5mg/kg i.p. d-tranylcypromine, l-tranylcypromine. The LD50-of pentobarbital was reduced to almost one half by d-tranylcypromine or dl-trancypromine, compared to the l-isomer. It is concluded that dl-trancypromine enhances pentobarbital toxicity by inhibiting metabolism of the drug. 11 references. (Author abstract modified)

**003479** Strasberg, S. M.; Kay, R. M.; Ilson, R. G.; Petrunka, C. N.; Paloheimo, J. E. Dept. of Surgery, Toronto Western Hospital, Toronto, Ontario, Canada **Taurolithocholic acid and chlorpromazine cholestasis in the rhesus monkey.** Canadian Journal of Physiology and Pharmacology. 57(10):1138-1147, 1979.

Cholestasis induced by taurolithocholic acid (TLC) and chlorpromazine (CPZ) were studied in rhesus monkeys. Results showed that TLC cholestasis occurs predominately at the canalicular level, whereas CPZ probably affects bile flow at the ductular level as well. Increased permeability to inulin was observed following administration of TLC or CPZ. Taurocholic acid protected the hepatocyte against the effects of CPZ and TLC. It is suggested that CPZ administration at times of high bile acid flux through the liver, as occurs shortly after meals, may reduce the incidence of CPZ cholestasis. 28 references. (Author abstract modified)

**003480** Strocchi, Paola; Novello, F.; Montanaro, N.; Stirpe, F. Mailman Research Center, McLean Hospital, Belmont, MA 02178 **Effect of intraventricularly injected ricin on protein synthesis in rat brain.** Neurochemical Research. 4(2):259-268, 1979.

Ricin, a protein from the seeds of Ricinus communis that inhibits protein synthesis by eukaryotic ribosomes, was highly toxic when injected intraventricularly to male Sprague-Dawley rats. The median lethal dose was 0.241mcg at 72 hours and 0.084mcg at 7 days; no animals died before 20 hours of intoxication. The poisoned animals showed signs of central depression prior to death. Incorporation of amino acids in vivo into brain total protein and into brain ribosomes was impaired, as was protein synthesis in vitro by microsomes isolated from the brains of poisoned rats. Since centrally administered ricin remains confined within the CNS, it may be a useful means of studying the effect of protein synthesis inhibition in brain, in the absence of peripheral effects. 25 references. (Author abstract modified)

**003481** Waterfall, J. F.; Smith, M. A.; Gaston, W. H.; Maher, J.; Warburton, G. Dept. of Pharmacology, Wyeth Institute of Medical Research, Huntercombe Lane South, Taplow, Maidenhead, England **Cardiovascular and autonomic actions of ciclazindol and tricyclic antidepressants.** Archives Internationales de Pharmacodynamie et de Therapie. 240(1):116-136, 1979.

The cardiovascular actions of ciclazindol, a novel antidepressant, were compared with those of nortriptyline, desipramine, imipramine, and amitriptyline. Ciclazindol had no significant effect on blood pressure in female rats in doses up to 25.6mg/kg i.v., but the other four drugs evoked significant decreases at doses of 0.8 to 1.6mg/kg. The hemodynamic and electrocardiogram changes induced by ciclazindol were minor compared to those seen with the other antidepressant drugs. Ciclazindol was equipotent with the tricyclics as a local anesthetic in skin wheal tests. In isolated tissues, ciclazindol showed no marked anticholinergic or antiserotonergic effects, but was weakly antihistaminic and potentiated responses to noradrenaline. Results suggest that ciclazindol is pharmacologically different from the traditional antidepressant drugs and may not produce the unwanted side-effects associated with clinical use of tricyclic antidepressants. 38 references. (Author abstract modified)

## 06 METHODS DEVELOPMENT

**003482** Dixon, Ross; Glover, William; Earley, James; Delaney, Michael. Research Division, Hoffmann-La Roche Inc., Nutley, NJ 07110 **Desmethyldiazepam: a specific radioimmunoassay.** Journal of Pharmaceutical Sciences. 68(11):1471, 1979.

A specific radioimmunoassay for desmethyldiazepam was developed. Comparison with an established electron capture gas/liquid chromatographic method for determination of desmethyldazpam revealed comparable specificity and precision for the two methods. Tricyclic antidepressants, which are commonly prescribed in conjunction with benzodiazepines, did not cross-react with the antiserum. 5 references.

**003483** Gray, D. Shaun; Gorzalka, Boris B. Dept. of Psychology, University of British Columbia, Vancouver, Canada V6T 1W5 **An easily constructed durable chronic intracerebral cannula system.** Pharmacology Biochemistry and Behavior. 11(4):463-466, 1979.

The construction of a simple, inexpensive, and rugged intracerebral cannula system suitable for use in rodents is described. The guide cannula assembly is molded from dental acrylic cement and has a protective acrylic collar surrounding the end of the actual guide cannula. This system appears to be superior to current methodologies in terms of expense, durability, and ease of construction. 10 references. (Author abstract modified)

**003484** Liebman, Frederick M.; Klinger, Gary. Dept. of Physiology, New York University, Dental Center, 421 First Avenue, New York, NY 10010 **In vivo hamster skeletal muscle preparation: morphine sensitive-naloxone insensitive.** European Journal of Pharmacology. 62(2/3):167-175, 1980.

The hamster cheek pouch retractor muscle preparation was evaluated as an in vivo assay model for morphine and naloxone. The average percent reduction in contractile force increased with increasing concentrations of morphine injected into the pouch. Unilateral injections of morphine did not affect the contralateral muscle. Opiate receptors in this preparation were relatively insensitive to naloxone. This assay system has potential for studies of opiates and related drugs, opiate tolerance and withdrawal, and pain modulation. 21 references. (Author abstract modified)

**003485** Littmann, K.; Heredia, J. Medrano; Hoffmeister, F. Chirurgische Klinik und Poliklinik der Universitat, Hufelandstr. 55, D-4300 Essen, Germany **/A new method for enteral self-administration of psychotropic drugs in the rhesus monkey./** Eine neue Methode zur enteralen Selbstverabreichung von psychotrop wirksamen Pharmaka beim Rhesusaffen. Arzneimittel-Forschung. 29(12):1888-1890, 1979.

A surgical method for the parenteral self-administration of psychoactive substances in the rhesus monkey is described. The process involves a modified gastrostomy with a catheter fixed to the inner wall of the abdomen. The catheter is placed subcutan-

eously, exits though a point between the shoulders, and is held in place with a leather corset. The method has been found to be safe for long-term use. 4 references. (Journal abstract modified)

**003486** Lotz, W.; Syllwasschy, B. F. Hoffman, La Roche & Co. Ltd., Pharma Research Dept., Basel, Switzerland **Release of oligopeptides from silicone rubber implants in rats over periods exceeding ten days.** Journal of Pharmacy and Pharmacology. 31(9):649-650, 1979.

A new method of peptide administration was developed, using silicone rubber implants in rats. Studies with luteinizing hormone releasing hormone and thyrotropin releasing hormone showed that the oligopeptides were released for at least 10 days after subcutaneous implantation. It is suggested that this method may be used to simulate basal secrection of other peptides, such as ACTH fragments and enkephalins. 2 references.

**003487** Malkinson, A. M.; Shere, W. C. School of Pharmacy, University of Colorado, Boulder, CO 80309 **Decreased pentobarbital sleeptime following a single intraperitoneal injection of cedar-derived sesquiterpenes.** Research Communications in Chemical Pathology and Pharmacology. 25(3):607-610, 1979.

Pentobarbital sleep time was reduced by 40% within 1 day of i.p. injection of cedar sesquiterpenes in male BALB/cByJ mice. The estimated median effective dose was 50mg/kg terpenes. The mice recovered from the terpene-induced reduction in the strength of hypnosis within 6 days of the terpene injection. The potency of the terpenes, the rapidity of their action, and the duration of their effectiveness in modulating drug response suggest they may be useful pharmacological tools. 12 references. (Author abstract modified)

**003488** Stein, E. A.; Rodd, D. Dept. of Biology, Marquette University, Milwaukee, WI 53233 **A new injection technique for intracerebral drug administration in behaving animals.** Pharmacology Biochemistry and Behavior. 12(5):815-817, 1980.

A new technique for administering drugs into the cerebral ventricles or brain tissue of awake, freely moving animals is described. The novel apparatus includes a fluid pump that can accurately deliver a predetermined amount of fluid (down to the nanomolar range) into the brain. The entire pump is mounted via electrical slip rings, which permit the pump to rotate and thereby eliminate the need for a fluid commutator. 5 references. (Author abstract modified)

**003489** Tokes, Zoltan A.; St. Peteri, Agnes Kulcsar; Todd, John A. Dept. of Biochemistry, School of Medicine, University of Southern California, Los Angeles, CA 90033 **Availability of liposome content to the nervous system. Liposomes and the blood-brain barrier.** Brain Research. 188(1):282-286, 1980.

Experiments in Swiss-Webster mice indicated that hydrophilic molecules entrapped in artifical lipid bilayer vesicles do not cross the blood-brain barrier and become available to the CNS. Following i.v. injection of liposome entrapped fluorescent labeled albumin, 6-carboxyfluorescein, and trypan blue, none of the entrapped substances penetrated anatomical regions of neural origin. No centrally mediated convulsive effects were seen after i.v. injection of liposome entrapped methylbicuculline. Peripheral but not central effects were observed after i.v. injection of liposome entrapped serotonin. Even after treatment with the bacterium Bordatella pertussis, which increases the permeability of the blood-brain barrier, none of the liposome entrapped substances showed increased availability to the CNS. 19 references.

**003490** Young, W. Scott, III; Kuhar, Michael J. Dept. of Pharmacology, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **A new method for receptor autoradiography: (3H)opioid receptors in rat brain.** Brain Research. 179(2):255-270, 1979.

A new method for light microscopic autoradiography of mounted tissue sections labeled in vitro is described. Opioid receptors are labeled with tritiated ligands in lightly fixed tissue sections mounted on microscope slides, and emulsion coated coverslips are attached to obtain the autoradiograms. This distribution of (3H)diprenorphine binding sites determined by this in vitro method in rat brain was identical to that found in earlier studies using in vivo labeling of opioid receptiors. The advantages of this method over traditional in vivo methods are discussed. 33 references. (Author abstract modified)

# CLINICAL PSYCHOPHARMACOLOGY

## 07 EARLY CLINICAL DRUG TRIALS

**003491** Gerner, Robert H.; Catlin, Don H.; Gorelick, David A.; Hui, Ka Kit; Li, Cho Hao. UCLA Neuropsychiatric Institute, 760 Westwood Plaza, Los Angeles, CA 90024 **Beta-endorphin: intravenous infusion causes behavioral change in psychiatric inpatients.** Archives of General Psychiatry. 37(6):642-647, 1980.

In a double-blind, placebo controlled crossover design, 10 depressed and eight schizophrenic inpatients were administered synthetic human beta-endorphin infusions, intravenously. Physicians' and nurses' ratings and patients' self-ratings were used to measure behavioral change. Depressed patients improved significantly 2 to 4 hr after beta-endorphin treatment. There was no significant change in the schizophrenic patients as a group, although six of eight worsened after beta-endorphin treatment. No significant behavioral effects were observed during the infusions themselves or on postinfusion days. 58 references. (Author abstract)

**003492** Thompson, Donald M. Dept. of Pharmacology, Georgetown University Schools of Medicine and Dentistry, Washington, DC 20007 **Selective antagonism of the rate-decreasing effect of d-amphetamine by chlorpromazine in a repeated-acquisition task.** Journal of the Experimental Analysis of Behavior. 34(1):87-92, 1980.

The possibility that the effects of d-amphetamine could be blocked by chlorpromazine was examined in a repeated acquisition task by pigeons. When d-amphetamine was adminsitered alone, the overall response rate decreased and the percent errors increased with increasing doses. When a small dose of chlorpromazine, which was ineffective when given alone, was adminsitered in combination with d-amphetamine, the rate decreasing effect was antagonized. The antagonism was selective in that the error increasing effect of d-amphetamine was augmented by chlorpromazine. The nature of the joint effect of the two drugs depends on the behavioral measure: rate versus accuracy. 13 references. (Author abstract modified)

## 08 DRUG TRIALS IN SCHIZOPHRENIA

**003493** Berger, P. A.; Watson, S. J.; Akil, H.; Elliott, G. R.; Rubin, R. T.; Pfefferbaum, A.; Davis, K. L.; Barchas, J. D.; Li, C. H. Stanford Mental Health Clinical Research Center, Ward 4C2, VA Medical Center, 3801 Miranda Ave., Palo Alto, CA 94304 **Beta-endorphin and schizophrenia.** Archives of General Psychiatry. 37(6):635-640, 1980.

The effects of beta-endorphin in chronic shcizophrenia were examined in nine male inpatients in a double-blind crossover comparison of a single intravenous 20mg injection of beta-endorphin and saline. Bolus injection of beta-endorphin from an albumin coated syringe produced markedly higher plasma concentrations than did slow intravenous infusion from a nonalbumin coated syringe. Beta-endorphin produced a significant increase in serum prolactin levels. In one patient, both 10mg morphine sulfate and 20mg beta-endorphin produced similar increases in the alpha power of the EEG. In eight patients, beta-endorphin administration was associated with a statistically significant, but not clinically obvious, improvement in schizophrenic symptoms. 54 references. (Author abstract)

**003494** Bigelow, Llewellyn B.; Zalcman, Steven; Kleinman, Joel E.; Weinberger, Daniel; Luchins, Daniel; Klein, Susan T.; Wyatt, Richard Jed. no address **Propranolol treatment of chronic schizophrenia: a controlled study. (Unpublished paper).** Washington, DC, NIMH, 1980. 1 p.

Propranolol was added to the neuroleptic regimen of 11 chronic schizophrenic pateients in a placebo controlled double-blind crossover study. This was an attempt to replicate Yorkston's reported success with propranolol in a series of chronically ill schizophrenic patients. The maximum does was 1920mg every 24 hours; some patients tolerated less. Behavioral status was measured by a modified BPRS completed daily by the nursing staff. An analysis of variance of the mean ratings of the nine patients who completed a minimum of 1 month on a high dose failed to show any effect for propranolol. Two subjects, however, improved significantly in some aspects of their pathology and were given repeat trials. In neither patient could the initially observed improvement be replicated. It is suggested that further trials may be indicated in slected subjects who show evidence of a high degree of noradrenergic activity. (Author abstract modified)

**003495** Bjerkenstedt, L.; Harnryd, C.; Sedvall, G. Bjerkenstedt: Psychiatry, Karolinska Hospital, Karolinska Institute, S-104 01 Stockholm, Sweden **Effect of sulpiride on monoaminergic mechanisms in psychotic women.** Psychopharmacology. 64(2):135-139, 1979.

Concentrations of the major monoamine metabolites homovanillic acid (HVA), 4-hydroxy-3-methoxyphenylethylene glycol (MOPEG), and 5-hydroxyindoleacetic acid (5-HIAA) were determined in lumbar cerbrospinal fluid (CSF) of 15 psychotic women with schizophrenic symptomatology before and 4 weeks after treatment with sulpiride (Dogmatil 200mg x 4). The metabolites were determined by a mass fragmentographic method. Prolactin concentrations in CSF and plasma were determined by radioimmunoassy. The clinical effects were evaluated by ratings according to the comprehensive psychopathology rating scale and a scale for side-effects. Levels of HVA and prolactin CSF and plasma were significantly elevated during treatment. No effects on concentrations of MOPEG or 5-HIAA were observed. The biochemical data indicate that clinical doses of sulpiride blocked dopamine receptors in the nigrostriatal pathway as well as in the tuberoinfundibular system. Treatment with sulpiride was associated with marked reduction in psychotic morbidity. 32 references. (Author abstract)

**003496** Brambilla, F.; Scarone, S.; Ponzano, M.; AFFEI, C.; Nobile, P.; Rovere, C.; Guastalla, A. Clinica Psichiatrica of Milano University, Via Besta 1, Milano Affori, Italy **Catecholaminergic drugs in chronic schizophrenia.** Neuropsychobiology. 5(4):185-200, 1979.

The effect of dopaminergic related and stimulatory drugs were examined in chronic hebephrenic schizophrenics untreated with neuroleptic drugs. The patients were assessed psychologically, and levels of follicle stimulating hormone (FSH), luteinizing hormone (LH), testosterone and growth hormone (GH) were assayed radiommunologically before, in the middle of, and after each course of therapy. Two patients showed improvement in the affective behavioral symptomatology during therapy, while the other four, who had a more severe degree of mental deterioration and destruction, were unchanged. FSH and LH levels, very low under basal conditions, did not change under therapy. Testosterone was very low before therapy and increased in only one subject. Normal basal GH levels increased during therapy in some of the patients, but not constantly. The results are discussed in relation to the catecholamine hypotheses of schizophrenia. 80 references. (Author abstract modified)

**003497** Capstick, Norman. Graylingwell Hospital, Chichester, West Sussex PO19 4PQ, England **Long-term fluphenazine decanoate maintenance dosage requirements of chronic schizophrenic patients.** Acta Psychiatrica Scandinavica. 61(3):256-262, 1980.

To investigate long-term fluphenazine decanoate maintenance dosage requirements of chronic schizophrenic patients, 47 schizophrenic outpatients were progressively withdrawn from the medication by increasing the time interval between injections while maintaining the amount of drug per injection. The rate of reduction varied with each patient depending on various factors such as environmental stress considerations and the patient's wishes. Finally three injections at 8 week intervals were given before complete withdrawal. In a 23.7 month followup period, a relapse rate of 80% was found with 25 patients relapsing during the withdrawal phase and 22 patients after the drug had been completely withdrawn. It is concluded that if a patient suffering from schizophrenia responds well to fluphenazine decanoate, then this drug will probably need to be continued on an indefinite basis with the minimum amount of drug being determined by trial and error. 7 references. (Author abstract modified)

**003498** Chouinard, Guy; Jones, Barry D. Dept. of Psychiatry, McGill University, Montreal, Quebec, Canada **Evidence of brain dopamine deficiency in schizophrenia.** Canadian Journal of Psychiatry. 24(7):661-667, 1979.

The proposal that the increased dopamine function suggested by the dopamine hypothesis of schizophrenia is a dopaminergic postsynaptic receptor supersensitivity resulting from a dopamine deficiency is presented. Three double-blind controlled studies conducted on drugs which alter brain dopaminergic activity in a manner different from that of classic neuroleptics are reported. It is concluded that currently accepted modes of pharmacological therapy are in the short-term controlling the dopamine supersensitivity secondary to a deficiency, but contributing in the long-term to increase the dopamine deficiency, and so exacerbate the supersensitivity. 38 references. (Author abstract modified)

**003499** Chowdhury, M. E. H.; Chacon, Carlos. Chacon: Psychiatric Unit, New Cross Hospital, Wolverhampton, England **Depot fluphenazine and flupenthixol in the treatment of stabilized schizophrenics. A double-blind comparative trial.** Comprehensive Psychiatry. 21(2):135-139, 1980.

Differences between fluphenazine decanoate and flupenthixol decanoate were studied in a double-blind crossover design trial involving a group of 22 schizophrenics maintained in the community. The results show no marked differences in the measured clinical response between the two drugs. Flupenthixol decanoate showed a good, statistically significant activiating action on work performance although its effect on mood seemed negligible. Fluphenazine decanoate proved to be more active on mood, producing mainly an increase of the elation score (selected Present State Examination items), and also improving (nonsignificantly) work performance. A simple measure of work performance appeared to be a good index of clinical state. In schizophrenics in the community, the pharmacologically active life of the depot neuroleptics could be longer than 4 weeks. 18 references. (Author abstract)

**003500** Cooper, Sam F.; Dugal, Robert; Elie, Robert; Albert, Jean-Marie. Institut National de la Recherche Scientifique, 7401 rue Hochelaga, Montreal H1N 3M5, Quebec, Canada **Metabolic interaction between amitriptyline and perphenazine in psychiatric patients.** Progress in Neuro-Psychopharmacology. 3(4):369-376, 1979.

Gas/liquid chromatography was used to determine the steady-state levels of amitriptyline (AT), nortriptyline (NT), and perphenazine (PPZ) in plasma samples from 65 schizophrenic patients treated with amitriptyline (150mg/day), perphenazine (20mg/day), or a combined regimen of 150 mg amitriptyline and 20 mg perphenazine. PPZ significantly increased the steady-state level of NT in plasma, probably through inhibition of the hydroxylation biotransformation pathway. PPZ had no effect on AT levels, indicating it has no effect on the desmethylation pathway or on the hydroxylation of AT. 26 references. (Author abstract modified)

**003501** Cox, Stephen M.; Ludwig, Arnold M. Ludwig: Dept. of Psychiatry, University of Kentucky, College of Medicine, Lexington, KY 40536 **Neurological soft signs and psychopathology: incidence in diagnostic groups.** Canadian Journal of Psychiatry. 24(7):668-673, 1979.

The performance of different groups of psychiatric patients with respect to individual neurological soft signs was studied. The potential influence of psychotropic drugs on the significant findings was also analyzed. The results show that specific individual neurological soft signs are significantly more frequently present in schizophrenics than in either controls or in other psychiatric groups. Additionally, there was no statistical evidence of psychotropic drug effects on the findings. 13 references. (Author abstract modified)

**003502** DAmato, Franco Colucci. Ospedale Psichiatrico Provinciale, Naples, Italy /**Comparative evaluation of the therapeutic action of fluphenazine decanoate with other drugs and of the possibility of clinical and social utilization.**/ Valutazione comparativa dell'azione terapeutica della flufenazina decanoato con altri farmaci, e delle possibilita di utilizzazione clinica e sociale. Rivista Sperimentale di Freniatria. 103(5);1561-1572, 1979.

The therapeutic effects of fluphenazine decanoate, haloperidol, clothiapine, and thioridazine were compared experimentally. Fifty schizophrenic patients were treated with fluphenazine decanoate and 50 patients were treated with haloperidol, clothiapine, and thioridazine. Optimum doses and administration regimens, possible side-effects, rapidity and duration of the patient's reinstatement to his everyday life, and the length of treatment as a hospital patient and as an outpatient were evaluated. Results indicate that the fluphenazine decanoate was best for rapidity and duration of reinstatement into everyday life, thioridazine presented the fewest side-effects in inpatients and outpatients. Special consideration was placed on the possibility of patient followup through outpatient services. 15 references. (Journal abstract modified)

**003503** Dongier, M. Dept. of Psychiatry, McGill University, 1025 Pine Avenue West, Montreal, Quebec, H3A 1A1, Canada **Neurosciences at the Allan Memorial Institute.** Trends in NeuroSciences. 2(5):10-11, 1979.

An overview of research achievements and current investigations in the neurosciences at the Allan Memorial Institute at McGill University, Montreal, Canada, is presented. In the area of psychopharmacology, work on depression and schizophrenia is being conducted. In studying the antipsychotic effects of medications that do not block dopaminergic receptors, neuroleptic drugs have been shown to induce a supersensitivity psychosis when used in long-term administration. The latest study on the therapeutic efficacy of tryptophan in depression has led to the suggestion that there is a therapeutic window for tryptophan in the treatment of unipolar depression, and bipolar depressed patients need higher doses. In the area of neurophysiology, the action of sensory afferents on motor behavior, the organization of the visual input into the motor cortex, and the effects of ad-

renal steroids on excitability are being explored. In the area of clinical neurophysiology, a sedation threshold had been helpful in diagnostic work, and reaction time experiments have revealed a sign of cerebral dysfunction called psychophysiology and neuropsychology, an important development was the recording of autonomic system functions of individuals in stressful interviews.

**003504** Donlon, Patrick T.; Hopkin, John T.; Tupin, Joe P.; Wicks, John J.; Wahba, Michel; Meadow, Arnold. Dept. of Psychiatry, School of Medicine, University of California, Davis Medical Center, 2315 Stockton Blvd., Sacramento, CA 95817 **Haloperidol for acute schizophrenic patients: an evaluation of three oral regimens.** Archives of General Psychiatry. 37(6):691-695, 1980.

The relative efficacy of three oral regimens of haloperidol was compared in a 10 day double-blind study of 63 acutely ill schizophrenic patients newly admitted to the hospital. One group of patients received 20mg haloperidol on day 1, then increasing increments of 20mg a day, reaching a maximum dosage of 100mg on day 5. Another group received 10mg haloperidol on day 10. A third group of patients received a fixed dosage of 10mg daily for 10 days. Haloperidol was well tolerated by the patients; there were no serious adverse reactions. The data indicated that the regimens had similar therapeutic efficacy, suggesting that acutely ill schizophrenic patients respond to a wide range of doses of haloperidol, but that onset of response and efficacy are not increased in most patients by providing a high initial loading. Adequate safe dosage must be determined in each case. 15 references. (Author abstract)

**003505** Eaton, Elaine M.; Busk, Jytte; Maloney, Michael P.; Sloane, R. Bruce; Whipple, Katherine; White, Kerrin. LAC-USC Medical Center, 1934 Hospital Place, Los Angeles, CA 90033 **Hemispheric dysfunction in schizophrenia: assessment by visual perception tasks.** Psychiatry Research. 1(3):325-332, 1979.

Before and after a double-blind trail of haloperidol vs. mesoridazine, 24 hospitalized schizophrenics performed visual perception tasks designed to assess function of the cerebral hemispheres. Tasks involved identifying as same or different two images projected tachistoscopically to the right or left visual field or to both together. Both before and after treatment, subjects responded most slowly and least accurately to letter matching. Bilateral presentation of stimuli resulted in faster and more accurate responses, except on shape matching. Neuroleptic treatment improved speed and accuracy overall, though not under certain task conditions. Results accorded more with an impairment in verbal processing and interhemispheric coordination than with a specific left hemispheric deficit in schizophrenia. 26 references. (Author abstract modified)

**003506** Fink, M.; Irwin, P.; Weinhold, P. PO Box 269, Great Neck, NY 11022 **EEG profile studies of clozapine in volunteers and psychiatric patients.** Pharmakopsychiatrie Neuro-Psychopharmakologie. 12(2):184-190, 1979.

EEG profile studies of clozapine in volunteers and in psychiatric patients are reported in a paper presented at the 1978 symposium eld in Basel Switzerland. In normal volunteers and in psychotic patients, clozapine elicited EEG effects which were more similar to those of sedative thymoleptic antidepressants than to those established for antipsychotic compounds. It is probable that the antipsychotic activity reported by some observers reflected the sedative qualities of the compound and not a prototypic antipsychotic activity. Further testing in other psychiatric populations, particularly patients with depressive illnesses, is warranted. 29 references. (Author abstract modified)

**003507** Fleischhauer, J. Kantonale Psychiatrische Klinik, CH-4915 St. Urban/Lu, Switzerland **High dosage treatment with fluphenazine intravenously followed by depot injections in acute schizophrenia.** International Pharmacopsychiatry. 15(1):6-13, 1980.

Thirteen acute schizophrenics were treated for 28 days first with fluphenazine infusion with doses up to 180mg on an average of 5 days followed directly by an injection of 25mg fluphenazine decanoate repeated after an average of 16 days. The clinical effectivity of the medium high infusion dose and the direct changeover from infusion to depot injection was examined. No serious side effects could be seen, the changeover happended without exacerbation of symptoms. The clinical effectivity came up to the usual therapy with normal dosage after 28 days therapy, a somewhat more rapid deliverance of symptoms during the first days remained impressive. 10 references. (Author abstract)

**003508** Gottschalk, Louis A.; Biener, Robert; Noble, Ernest P.; Birch, Herman; Wilbert, Donald E.; Heiser, Jon F. Dept. of Psychiatry and Human Behavior, College of Medicine, University of California at Irvine, Irvine, CA 92664 **Thioridazine plasma levels and clinical response.** In: Gottschalk, L., The content analysis of verbal behavior. New York, SP Medical & Scientific Books, 1979. 977 p. (p. 455-469).

The relationship of a single, oral dose of a phenothiazine derivative, thioridazine, to the resulting drug blood levels and clinical responses in acute schizophrenics was examined. Following the single dose of thioridazine, a significant average decrease was noted within 24 hours in the social alienation/personal disorganization scores. The manifestations of the schizophrenic syndrome showing such significant improvement included thought disorder, conceptual disorganization, apathy, anxiety, and depression. Significant correlations were found between indices of plasma thioridazine levels and favorable clinical responses on certain behavioral and psychological features of the schizophrenic syndrome. 28 references. (Author abstract modified)

**003509** Gottschalk, Louis A.; Gleser, Goldine C.; Cleghorn, John M.; Stone, Walter N.; Winget, Carolyn N. Department of Psychiatry and Human Behavior, College of Medicine, University of California, Irvine, CA 92664 **Predicition of changes in severity of the schizophrenic syndrome with discontinuation and the administration of phenothiazines in chronic schizophrenic patients: language as a predictor and measure of change in schizophrenia.** In: Gottschalk, L., The content analysis of verbal behavior. New York, SP Medical & Scientific Books, 1979. 977 p. (p. 349-366).

Possible predictors of change in the severity of the schizophrenic syndrome among schizophrenic patients with cessation and administration of phenothiazine chemotherapy were examined. The intercorrelations among content analysis scores of the speech of schizophrenics indicate that anxiety, overt hostility outward, and ambivalent hostility are associated with high social alienation/personal disorganization scores. It is suggested that these correlations signify that the sicker schizophrenics are more likely to manifest their disorder in open, destructive aggression, in paranoid ideation, or in higher anxiety. Furthermore, the verbal sample technique for assessing behavior appears to offer a fruitful method for following longitudinal changes in the magnitude of the schizophrenic syndrome and in finding predictors of trend with various types of therapy. 34 references.

**003510** Haase, H. J.; Kaumeier, S.; Schwarz, S.; Gundel, A.; Linde, O. K.; Bomhard, R. Honess; Rauwolf, E. R.; Scheel, R.;

Seyfferth, H. V. Kalmusweg 11, D-6701 Neuhofen, Germany **Clinical trial for droperidol for the determination of the neuroleptic threshold and the neuroleptic-therapeutic range.** International Pharmacopsychiatry. 15(1):74-80, 1980.

In an open study involving 30 schizophrenic patients the neuroleptic threshold dose, measured using Haase's graphopathological test, and the maximum dose were determined. The neuroleptic threshold dose was 18.5mg/day, the maximum dose was 38.2mg/day. With reference to the effectiveness, good to very good results were obtained in 15 cases. Ten patients complained of extrapyramidal disturbances, which was to be expected in view of the study design aimed at the determination of the maximum dose. 7 references. (Author abstract)

**003511** Hanssen, Tora; Heyden, Thomas; Sundberg, Inez; Alfredsson, Gunnel; Nyback, Henrik; Wetterberg, Lennart. Wetterberg: Dept. of Psychiatry, Karolinska Institute, Box 12500, S-112 81 Stockholm, Sweden **Propranolol in schizophrenia: clinical, metabolic, and pharmacological findings.** Archives of General Psychiatry. 37(6):685-690, 1980.

Six schizophrenic patients were administered propranolol hydrochloride to evaluate pharmacological, endocrinological, and antipsychotic properties of the drug. They had previously been unsuccessfully treated with phenothiazines. After a drug free period of 2 weeks, propranolol was administered in gradually increasing doses. After 2 to 4 weeks, a low dose of phenothiazines was added. The clinical effect was evaluated using the Comprehensive Psychopathological Rating Scale. Three of six patients showed a definite improvement with propranolol therapy given as a sole treatment. Propranolol in plasma was positively related to dosage. The proportion of its major metabolite, 4-hydroxypropranolol, decreased with increasing drug dose. Melatonin and prolactin levels in serum decreased noticeably with propranolol treatment. When phenothiazines were added, prolactin increased above drug free levels. These results support the view that propranolol has an antipsychotic potential that needs further evaluation in clinical trials. 38 references. (Author abstract)

**003512** Hymowitz, Paul; Spohn, Herbert. New York Hospital, Cornell Medical Center, 21 Bloomingdale Road, White Plains, NY 10605 **The effects of antipsychotic medication on the linguistic ability of schizophrenics.** Journal of Nervous and Mental Disease. 168(5):287-296, 1980.

To examine the effects of antipsychotic medication on the linguistic ability of schizophrenics, 22 chronic patients were tested on medication and again in a drug free period. Ss were matched with a group of patients who remained on medication. Speech in response to interview questions and TAT cards was analyzed via linguistic measures to assess the effects of neuroleptic drugs on communication ability. Results indicate that medicated patients are more verbally communicative and show an increase in the complexity and coherence of their speech and a decrease in pathological utterances. The findings suggest that drug treatment can enhance such patients' capacity to use verbally oriented psychotherapy. 21 references. (Author abstract modified)

**003513** Johnson, D. A. W. University Hospital of South Manchester, West Didsbury, Manchester 20, England **Further observations on the duration of depot neuroleptic maintenance therapy in schizophrenia.** British Journal of Psychiatry. 135(December):524-530, 1979.

Two patient samples (n=56 and n=91 schizophrenics), with different criteria for selection, were surveyed following discontinuation of depot neuroleptic (fluphenazine and flupenthixol) maintenance therapy. The patients had previously remained in a steady mental state on depot injections for periods varying between 1 and 4 years. Both the rates of relapse and patterns of relapse suggest that patients responding to medication needed to remain on maintenance therapy for a minimum of 4 years. The results further suggest that in chronic schizophrenics the drugs only suppress symptoms and that the prognosis following discontinuation of medication is substantially unchanged by increased duration of medication even after 4 years. The possibility of using short-term drug holidays to reduce risk of unwanted side-effects was also explored: after only 3 months without drugs, the risks of relapse were significantly increased. 13 references. (Author abstract)

**003514** Joseph, M. H.; Baker, H. F.; Johnstone, Eve C.; Crow, T. J. Division of Psychiatry, Clinical Research Centre, Watford Road, Harrow HA1 3UJ, England **3-Methoxy-4-hydroxyphenylglycol excretion in acutely schizophrenic patients during a controlled clinical trial of the isomers of flupenthixol.** Psychopharmacology. 64(1):35-40, 1979.

Urinary 3-methoxy-4-hydroxyphenylglycol (MHPG) excretion in 16 female and 21 male patients with acute schizophrenia was studied before and during a controlled clinical trial of the isomers of flupenthixol and placebo. Pretrial MHPG excretion was not related to severity of illness before the trial or to other pretrial clinical variables. In male subjects, higher pretrial MHPG excretion was associated with better outcome at 1 year posttrial. However, in females, no relationship between MHPG excretion and outcome was established. During the trial there was a reduction in MHPG excretion in patients treated with beta-flupenthixol, but no decrease in patients treated with alpha-flupenthixol or chlorpromazine. In patients on placebo, there was a reduction in MHPG excretion in those who did clinically well, but not in those who did poorly. Thus, low MHPG excretion may be a predictor of poor outcome in schizophrenia; MHPG excretion also changes both as a function of clinical state and of neuroleptic drug administration. 35 references. (Author abstract)

**003515** Jus, K.; Jus, A.; Villeneuve, A.; Pires, P.; Fontaine, P. Clinical Research Unit, Dept. of Psychiatry, Centre Hospitalier Robert Giffard, Beauport, Quebec, Canada **The utilization of hypnotics in chronic schizophrenics: some critical remarks.** Biological Psychiatry. 14(6):955-960, 1979.

The withdrawal and/or reduction of hypnotic medications in a sample of 23 chronic schizophrenic inpatients is described, and practices concerning the utilization of hypnotics in chronic schizophrenia are evaluated. Of 23 hospitalized chronic schizophrenic patients, all under neuroleptic medication, hypnotics taken previously for a long time could be totally withdrawn in 16 cases, and in 7 cases, the dosage was diminished by 30% without any sleep impairment. The gradual reduction of hypnotics was accompanied by a shift of neuroleptic dosage to the evening and bedtime, with reduction of the morning and midday dose, without change of the total daily dose. A significant improvement in the psychic state was observed in 16 patients after withdrawal of the hypnotic; seven patients showed a slight improvement after reduction of the hypnotic. It is contended that monthly or bimonthly reassessment of insomnia in the hospitalized population of chronic schizophrenics is indispensable to avoid the deleterious effects and abuse of hypnotic drugs. 7 references. (Author abstract modified)

**003516** Kane, John M.; Rifkin, Arthur; Quitkin, Frederic; Nayak, Devdutt; Saraf, Kishore; Ramos-Lorenazi, Jorge R.; Klein, Donald F.; Sachar, Edward J. Long Island Jewish-Hillside Medical Center, P. O. Box 38, Glen Oaks, NY 11004 **Low dose fluphenazine decanoate in maintenance treatment of schizophrenia.** Psychiatry Research. 1(3):341-348, 1979.

To test the clinical efficacy of low dose fluphenazine decanoate (1.25mg to 5.0mg biweekly) two experiments were carried out. An open trial was performed in 57 schizophrenic outpatients, lasting 6 months and a double-blind placebo controlled discontinuation study was performed in a subgroup of patients who maintained good remission throughtout the entire 6 month open trial. The results suggest that lower doses of fluphenazine decanoate than those usually administered may be effective in preventing psychotic relapse while keeping total cumulative dosage to a minimum. 24 references. (Author abstract)

**003517** Knights, Angela; Okasha, M. S.; Salih, Mohamed Ali; Hirsch, S. R. Dept. of Psychiatry, Charing Cross Hospital, London W6 8RF, England **Depressive and extrapyramidal symptoms and clinical effects: a trial of fluphenazine versus flupenthixol in maintenance of schizophrenic out-patients.** British Journal of Psychiatry. 135(December):515-523, 1979.

Depressive and extrapyramidal symptoms and clinical effects were evaluated in 57 schizophrenic patients started on either fluphenazine decanoate or flupenthixol decanoate injections just prior to discharge into the community. During the 6 month followup, 30% dropped out of treatment. Of those observed for 6 months, 7% relapsed, 54% experienced depressive symptoms, and 88% experienced extrapyramidal side-effects. Analysis of both clinical data and depressive and extrapyramidal ratings failed to discriminate between the two drugs. 19 references. (Author abstract modified)

**003518** Koukkou, Martha; Angst, J.; Zimmer, D. Research Dept., Psychiatric University Hospital, CH-8029 Zurich, Switzerland **Paroxysmal EEG activity and psychopathology during the treatment with clozapine.** Pharmakopsychiatrie Neuro-Psychopharmakologie. 12(2):173-183, 1979.

Results of a study of EEG effects and psychopathological changes in schizophrenia during treatment with clozapine (n=20) and haloperidol (n=19) are reported. Doses were adjusted to patients' needs, and data were collected on days 0, 3, 10, 20, and 30. Paroxysmal EEG patterns during a 20 min recording were counted in six scalp areas; 12 syndromes were assessed using the AMP system. Several schizophrenic and depressive syndromes showed a similar response to both drugs. On days 3, 10, and 20, more clozapine than haloperidol patients showed paroxysmal EEG patterns. Clozapine patients with paroxysmal patterns had received a lower dosage on 10 days than those without paroxysmal activity, and showed a greater reduction of the retarded depressive syndrome on day 20. There was a negative correlation between frequency of EEG paroxysms and intensity of depressive syndrome and a positive correlation between frequency of EEG paroxysms and reduction of the depressive syndrome with time. 28 references. (Author abstract modified)

**003519** Luchins, Daniel J.; Weinberger, Daniel R.; Kleinman, Joel E.; Neckers, Leonard; Rosenblatt, Jack E.; Bigelow, Llewellyn B.; Wyatt, Richard J. Division of Special Mental Health Research, William A. White Bldg., Rm. 536, St. Elizabeths Hospital, Washington, DC 20032 **Human leukocyte antigen A2 and psychopathology in chronic schizophrenia.** American Journal of Psychiatry. 137(4):499-500, 1980.

The relationship between human leukocyte antigen A2 and response to neuroleptic treatment was examined with 17 patients with chronic schizophrenia. Nine patients had A2 and eight did not. No evidence that schizophrenic patients with A2 respond less well to neuroleptic treatment than those without A2 was found. Results suggest that when chronic schizophrenic patients are drug free, those with A2 are less symptomatic than those without A2, a difference that is obscured by neuroleptic treatment. 10 references.

**003520** Maurer, Y. A. Psychiatrische Klinik Sanatorium Kilchberg, CH-8802 Kilchberg/Zurich, Switzerland /**Comparative investigation of action and side-effects in intravenous, intramuscular and oral application of fluphenazine dihydrochloride.**/ Vergleichende Untersuchung von Wirkung und Nebenwirkung bei intravenoser, intramuskularer und oraler Applikation von Fluphenazin Dihydrochlorid. Pharmakopsychiatrie Neuro-Psychopharmakologie. 12(5):366-374, 1979.

A comparative investigation of the effects and side-effects of fluphenazine dihydrochloride administered to 51 acutely diseased schizophrenics via the intravenous, intramuscular, and oral routes is presented. In addition, the relations between the age of the patients, duration of previous hospitalization, and the effects achieved with three application forms were considered. Patients suffering from acute schizophrenia are subjected to treatment according to different therapy standards, depending on the individual hospital. 4 references. (Journal abstract modified)

**003521** Meyers, Beverly; Tune, Larry E.; Coyle, Joseph T. Coyle: Dept. of Pharmacology, Johns Hopkins University School of Medicine, 725 N. Wolfe St., Baltimore, MD 21205 **Clinical response and serum neuroleptic levels in childhood schizophrenia.** American Journal of Psychiatry. 137(4):483-484, 1980.

The correlation between clinical response in childhood schizophrenia and serum levels of haloperidol was examined in a 13-year-old boy with a 2 year history of illness. Therapeutic response to neuroleptics coincided with serum levels greater than 50ng/ml of chlorpromazine equivalents. Serum levels of haloperidol fell markedly in the patient, and symptoms recurred rapidly after dose reduction. It is suggested that some children may metabolize neuroleptics more rapidly than adults; drug level measurement may be quite helpful in the effective management of childhood schizophrenia. 10 references.

**003522** Naber, D.; Finkbeiner, C.; Fischer, B.; Zander, K.-J.; Ackenheil, M. Ackenheil: Psychiatrische Klinik, Universitat Munchen, Nussbaumstrasse 7, D-8000 Munich 2, Germany **Effect of long-term neuroleptic treatment on prolactin and norepinephrine levels in serum of chronic schizophrenics: relations to psychopathology and extrapyramidal symptoms.** Neuropsychobiology. 6(4):181-189, 1980.

The effects of long-term neuroleptic treatment (5 to 25 years) on serum prolactin (Prl) and norepinephrine (NE) levels were examined in 23 male and 35 female chronic schizophrenic inpatients. Estimation of serum Prl and NE showed no elevation of Prl levels in either men or women. NE levels were distinctly elevated in both sexes: in men up to 0.77 plus or minus 0.04ng/ml; in women up to 0.90 plus or minus 0.48ng/ml. This elevation was induced by neuroleptic treatment rather than by external factors. No significant correlation to duration or dosage of neuroleptic treatment, psychopathological syndromes, and occurrence of tardive dyskinesia or parkinsonian side-effects could be seen; although a significant relationship between dosage or duration of anticholinergic treatment and the severity of tardive dyskinesia was found in men. The development of tolerance of the tuberoinfundibular dopamine system is discussed. 54 references. (Author abstract modified)

**003523** Nair, N. P. V.; Lal, S.; Cervantes, P.; Yassa, R.; Guyda, H. Lal: Dept. of Psychiatry, Montreal General Hospital, Montreal, Quebec, H3G 1A4 Canada **Effect of clozapine on apomorphine-induced growth hormone secretion and serum prolactin concentrations in schizophrenia.** Neuropsychobiology. 5(3):136-142, 1979.

The effect of clozapine on apomorpine-induced growth hormone secretion and serum prolactin concentrations was investigated in 10 schizophrenic patients. Clozapine had no effect on basal serum growth hormone concentrations, but significantly inhibited the apomorphine-induced growth hormone increase that occurred in seven Ss. Clozapine caused a slight (17%) but significant elevation in basal serum prolactin levels. These data suggest that in man clozapine, like other neuroleptics, blocks dopamine receptors, at least in the hypothalamic/pituitary axis. 53 references. (Author abstract modified)

**003524** no author. no address **Use of antidepressants in schizophrenia.** British Medical Journal. No. 6220:1037-1038, 1980.

Studies in the use of antidepressants in the treatment of schizophrenia are summarized. In 37 schizophrenic inpatients, 20 had depression at some time and symptoms improved as frequently in patients who received no antidepressant medication as in those who did. An incidence of 6% to 25% of depression was reported in a study of 284 patients. Improvement in treatment scores of 58 schizophrenics given perphenazine after a 2 week washout period was significantly greater than in 29 given placebo; addition of amitryptaline to the perphenazine regimen did not enhance clinical efficacy. A study of 35 schizophrenic outpatients with depressive symptoms showed symptom improvement when treated with perphenazine and amitriptyline. In another study, chlorpromazine alone appeared to be as effective as chlorpromazine plus amitriptyline. Improvement of extrapyramidal symptoms was significant in 21 of 30 inpatients given imipramine, although parkinsonism was worsened in those patients with severe symptoms. The effectiveness of lithium in schizophrenia has not been adequately assessed; however, there is some evidence suggesting its use for depressed type schizoaffective patients. 17 references.

**003525** Ragheb, M.; Berney, S.; Ban, T. Tennessee Neuropsychiatric Institute, Clinical Research Service, Middle Tennessee Mental Health Institute, Nashville, TN 37217 **Naltrexone in chronic schizophrenia: results of a clinical trial.** International Pharmacopsychiatry. 15(1):1-5, 1980.

A 4 week clinical trial, including a 1 week placebo washout period, assessed the antipsychotic activity of naltrexone in newly admitted, actively hallucinating, chronic schizophrenics. Chronic naltrexone administration was found to benefit two patients and to be of no value in three patients. Responsive patient differed from nonresponders by the presence of hallucinations despite adequate neuroleptic maintenance therapy and an appropriate response to pathological hallucinatory experience. On the basis of these findings, the possibility of a naltrexone responsive schizophrenic subgroup was considered. 12 references. (Author abstract)

**003526** Rosen, Alexander J.; Tureff, Steven E.; Daruna, Jorge H.; Johnson, Paul B.; Lyons, John S.; Davis, John M. Dept. of Psychology, University of Illinois at Chicago Circle, Chicago, IL 60680 **Pharmacotherapy of schizophrenia and affective disorders: behavioral correlates of diagnostic and demographic variables.** Journal of Abnormal Psychology. 89(3):378-389, 1980.

Time sampled observations were made of objectively defined ward behaviors in schizophrenic, affective, and schizoaffective patients during baseline and medication periods. Schizophrenics displayed less scanning, social interaction, participation, and laughing/smiling. The behavioral measures were relatively insensitive to demographic variables and were strongly dependent on environmental context, but did not change greatly over time for the major diagnostic categories in spite of pharmacological interventions that included therapeutic doses of antipsychotic, antidepressant, and antimanic drugs. Within diagnostic categories, however, patient clusters were extracted on the basis of amount and direction of behavior change. For affective patients, differential change was predictable from baseline response frequencies. The findings have implications for studies of dose response and rate dependence effects of psychotropic drugs in clinical populations and may help resolve the responder/nonresponder controversy in pharmacopsychiatry. 51 references. (Author abstract modified)

**003527** Shepherd, Michael. Institute of Psychiatry, Denmark Hill, London SE5 8AF, England **Medico-social evaluation of the long-term pharmacotherapy of schizophrenia: comparative study of fluphenazine and pimozide.** Progress in Neuro-Psychopharmacology. 3(4):383-389, 1979.

A study of a representative group of schizophrenic patients showed that oral pimozide, administered once daily, was at least as effective as parenteral fluphenazine decanoate in continuation treatment during the months following discharge. The main clinical criteria were occurrence and rate of schizophrenic relapse, depressive symptomatology, unwanted drug effects, and drug compliance. The pimozide treated patients also showed better social adjustment and functioned more effectively than the fluphenazine treated patients. 12 references. (Author abstract modified)

**003528** Singer, L.; Croisy, E.; Kapfer, Th. Service de Psychiatrie II, C.H.U. de Strasbourg, F-67005 Strasbourg Cedex, France /**Amoxapine and schizophrenia: on a study of 20 chronic schizophrenics.**/ Amoxapine et schizophrenie: a propos d'un essai comprenant 20 schizophrenes a evolution au long cours. Annales Medico-Psychologiques. 137(6-7):589-594, 1979.

The effects of amoxapine, an antidepressant which is a dibenzooxazepine, were examined in 20 chronic schizophrenics. Ss were given a dose varying from 75mg to 30mg per day for a month. The drug proved to have a strong disinhibiting effect, a lesser effect on agitation, and no effect on anxiety, delirium, or depression. The clinical condition generally improved in some cases, was about the same in other cases of patients previously treated with neuroleptics, and deteriorated in other cases of patients treated with some other compound. It is concluded that amoxapine has an effect similar to that of neuroleptics, but cannot be put in the same category, because secondary effects did not show any sign of the extrapyramidal series. A discussion follows the text of the article. 6 references. (Journal abstract modified)

**003529** Stauning, J. A.; Kirk, L.; Jorgensen, A. Jorgensen: Biochemical Dept., H. Lundbeck and Co. A/S, Ottiliavej 7-9, DK-2500 Copenhagen-Valby, Denmark **Comparison of serum levels after intramuscular injections of 2 percent and 10 percent cis(Z)-flupentixol decanoate in Viscoleo to schizophrenic patients.** Psychopharmacology. 65(1):69-72, 1979.

The serum concentrations of cis(Z)-flupentixol after injection of 2% and 10% cis(Z)-flupentixol decanoate in Viscoleo were investigated in a crossover study with eight schizophrenic patients. No statistically significant difference was found between the two preparations when the data from individual days or areas under the serum concentration curves were considered. For the individual patients a difference was found between the two treatments in six cases; one preparation gave the higher serum concentration in four cases and the other preparation in two cases. Thus, the difference found within individual patients reflects the intraindividual variation rather than a difference between preparations. The maximum serum concentration was seen at 4 or 7 days after injection. The maximum/minimum fluctuation ratio indicates that dosage intervals longer than 2 weeks seem reasonable for most of the patients. The similarity in the



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serum concentrations, no matter which concentration of flupentixol decanoate solution was given, indicates that a dispersal and possibly a metabolic breakdown of the oil depot takes place in the muscle. 10 references. (Author abstract)

**003530** Tamminga, C. A.; Schaffer, M. H. Experimental Therapeutics Branch, NINCDS, NIH, Bethesda, MD **Treatment of schizophrenia with ergot derivatives.** Psychopharmacology. 66(3):239-242, 1979.

The effect of DA agonists on schizophrenic symptoms was evaluated using the ergot alkaloids bromocriptine and CF25-397. Psychosis failed to improve in response to either drug at the relatively low doses administered. Unlike the antipsychotic property of apomorphine at low dose levels, neither of these ergot drugs improved schizophrenic symptomatology. Sugestions are made for further research. 27 references. (Author abstract modified)

**003531** Tegeler, J.; Floru, L. Rheinische Landesklinik, Psychiatrische Klinik der Universitat Dusseldorf, Bergische Landstr. 2, D-4000 Dusseldorf 12, Germany **/A comparative study of the long-acting neuroleptics perphenazine-enanthate and fluspirilene./** Eine vergleichende Untersuchung der Depot-Neuroleptika Perphenazin Onanthat und Fluspirilen. Pharmakopsychiatrie Neuro-Psychopharmakologie. 12(5):357-365, 1979.

The clinical profile and side-effects of perphenazine-enanthate and fluspirilene were compared in 45 female chronic schizophrenic patients. Over a 4 month period the psychopathological and somatic symptoms of the patients were evaluated by means of the AMP system and the self-evaluation scale PD-S. The antipsychotic effect of both drugs was similar concerning the paranoid, the hallucinatory deintegrative, and the catatonic syndromes. A significant difference with regard to perphenazine-enanthate was found in the AMP syndromes of hostility, hypochondria, and autonomic symptoms. The more pronounced sedative effect of perphenazine-enanthate can be recommended in hostile and restless schizophrenic patients, whereas fluspirilene is preferred for inactive autistic patients. 13 references. (Journal abstract modified)

**003532** Vranckx-Haenen, J.; De Munter, W.; Heykants, J. Psychiatric Hospital of the Alexian Brothers, Veldbornstraat 39, B-3300 Tienen, Belgium **Fluspirilene (Imap) administered in a biweekly dose for the prevention of relapses in chronic schizophrenics.** Acta Psychiatrica Belgica. 79(4):459-474, 1979.

Sixteen stabilized chronic schizophrenics treated with conventional long-acting neuroleptics were transferred to the long-acting neuroleptic-fluspirilene. The antipsychotic activity of fluspirilene was at least equal to that of the previous medication of conventional long-acting neuroleptics. In the majority of the patients the drug had a pronounced psychoreactivating effect. It is concluded that a high dose of fluspirilene can be administered biweekly without any loss of activity even at the end of the second week of trial administration. Clinical results are confirmed by plasma levels of fluspirilene. 12 references. (Author abstract modified)

**003533** Weinberger, Daniel; Bigelow, Llewellyn; Klein, Susan; Wyatt, Richard Jed. St. Elizabeths Hospital, NIMH, Washington, DC 20032 **Neuroleptic-induced supersensitivity psychosis in chronic schizophrenics. (Unpublished paper).** Washington, DC, NIMH, 1980. 1 p.

The clinical effects of neuroleptic withdrawal in 20 symptomatic chronic schizophrenic inpatients on long-term neuroleptic therapy were studied. The patients were withdrawn from drugs (with placebo substituted in 16 cases) and maintained drug free for 4 weeks. It was hypothesized that supersensitivity psychosis would manifest as an initial phase of significant symptomatic exacerbation followed by significant improvement. Thirteen patients got significantly worse, five showed no change, and two improved. The clinical course of four patients was consistent with the hypothesized course of supersensitivity psychosis; one of these showed overall improvement. No patient showed the inverse of this hypothesized course (initial improvement followed by relapse), which might have been expected if this pattern were a random variation. This study provides some clinical support for the existence of supersensitivity psychosis. (Author abstract modified)

**003534** Weizman, Ronit; Weizman, Avraham; Tyano, Sam; Wijsenbeek, Henricus; Ben David, Menashe. Geha Psychiatric Hospital, Beilinson Medical Center, Petah Tiqva, Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel **The biphasic effect of gradually increased doses of diazepam on prolactin secretion in acute schizophrenic patients.** Israel Annals of Psychiatry and Related Disciplines. 17(3):233-240, 1979.

The clinical antipsychotic activity of diazepam in schizophrenic patients was evaluated. Seven acute schizophrenic patients were treated with diazepam in gradually increased doses. The effects on serum prolactin levels and on the clinical improvement of these patients, evaluated by the Brief Psychiatric Rating Scale, were studied. During the entire period no clinical improvement was observed as measured by the scale. However, it is possible that initial doses of diazepam maintained for a minimum trial period of two weeks, might result in some significant improvement. 16 references. (Author abstract modified)

**003535** Winter, E.; Grosse, R. Psychiatrisches Landeskrankenhaus, D-7102 Weinsberg, Germany **/On the effect of biperiden in the treatment of acute schizophrenic stupor./** Zur Wirkung von Biperiden bei akuten substuporos-stuporosen Zustanden. Pharmakopsychiatrie Neuro-Psychopharmakologie. 12(5):383-387, 1979.

The intravenous application of biperiden to six patients with acute hypokinetic reaction suffering from schizophrenia of the paranoid hallucinatory type is reported. In all six cases a fast abolition of the stupor could be observed. The pathophysiological mechanisms deriving from the clinical experiences are discussed. A therapeutic procedure is suggested to treat acute schizophrenic stupor merely with drugs. 22 references. (Journal abstract)

**003536** Woggon, Brigitte; Bickel, P.; Schnyder, B. Psychiatrische Universitatsklinik Zurich, Forschungsdirektion, Lenggstrasse 31, Postfach 68, CH-8029 Zurich, Switzerland **/Discontinuation of antipsychotic drugs in chronic schizophrenic patients. II. Psychological and psychopathological test differences between patients with and without relapse./** Neuroleptika-Absetzversuche bei chronisch schizophrenen Patienten. II. Testpsychologische und psychopathologische Unterschiede zwischen Patienten mit und ohne Ruckfall. International Pharmacopsychiatry. 14(5):278-293, 1979.

Psychological and psychopathological differences between patients with or without relapse following a 4 week examination of neuroleptic drug discontinuation were examined in 30 chronic schizophrenic inpatients. Of these, 10 showed a significant increase in symptomatology which made resumption of therapy necessary. Before the discontinuation of treatment, the group of patients with later relapse and the group without relapse showed only slight differences in psychopathological symptoms, but significant differences in psychological test performances (reaction time concentration, fluency, etc. ). After 2 weeks without medication, a pronounced impairment of performance was found in patients with later relapse, At this time, the groups

showed no further significant differences in psychological test performance, but significant differences in psychopathological symptoms had developed. 25 references. (Journal abstract modified)

## 09 DRUG TRIALS IN AFFECTIVE DISORDERS

**003537** Amsterdam, J. D.; Winokur, A.; Mendels, J.; Snyder, P. University of Pennsylvania School of Medicine, Philadelphia, PA 19104 **Distinguishing depression subtypes by thyrotropin response to TRH testing.** Lancet. No. 8148:904-905, 1979.

Diminished thyrotropin (TSH) response to thyrotropin releasing hormone (TRH) was examined in 12 patients who met research diagnostic criteria for either unipolar or bipolar depression and the results are reported in a letter to the editor. All patients had Hamilton depression ratings of greater than 16 and had been off drugs for at least 7 days. Six age matched controls were included in the investigation. There were no significant differences in baseline T3, T4, and TSH among the three groups. After administration of TRH, no differences were observed for delta TSH between the unipolar group and the bipolar depressed group. Both groups demonstrated a delta TSH that was slightly, but not significantly, lower than that of the controls. The report of Gold et al. (1979) of significant differences in the TSH response to TRH between unipolar and bipolar depressed patients is not confirmed. 6 references.

**003538** Amsterdam, J.; Brunswick, D.; Mendels, J. V.A. Medical Center (151E,) University and Woodland Aves., Philadelphia, PA 19104 **The clinical application of tricyclic antidepressant pharmacokinetics and plasma levels.** American Journal of Psychiatry. 137(6):653-662, 1980.

A clinical approach for predicting and using plasma concentrations of tricyclic antidepressants in the treatment of depressed patients is presented. The pharmacokinetics of this groups of drugs and their side-effects and toxicity are reviewed. A therapeutic range for plasma concentrations of imipramine, amitriptyline, and nortriptyline is suggested. However, more definitive studies are needed to determine the necessary plasma levels for achieving clinical response with the other tricyclic antidepressants (desmethylimipramine, protriptyline, doxepin, clomipramine, imipramine N-oxide, and butriptyline). It is concluded that a more thorough knowledge of the clinical pharmacokinetics of tricyclic antidepressants should lead to more rational use of these drugs with a higher response rate and fewer adverse reactions. 95 references. (Author abstract modified)

**003539** Basso, P.; Gallo, V.; Montanini, R.; Vanzulli, F. Divisione Neurologica, Ospedale Provinciale Generale di Gallarate, Gallarate, Italy /**Antidepressive therapy with maprotiline (sequential parenteral/oral administration)**./ Terapia antidepressiva con maprotilina (schema sequenziale parenterale-orale). Rivista Sperimentale di Freniatria. 103(5);1573-1586, 1979.

The use of maprotiline in the treatment of various types of depression was studied. The sample of 40 patients (14 male and 26 female) was administered maprotiline intravenously, 50 to 100mg daily by drip infusion, during the first week and then by the oral route, 100 to 200mg daily. Results show that after clinical evaluation the patients demonstrated considerable improvement in the depressive symptoms after the first week of treatment, with further improvement at the end of the second week, after changing the type of administration. This dosage administration, intravenously and then orally, was responsible for the rapid action, more so than when the drug was only administered orally. The drug also demonstrated good tolerance. 20 references. (Journal abstract modified)

**003540** Botter, P. A. Sinai Clinic, Psychiatric Hospital of the Central Union for Jewish Mental Health, 23, Laan 1914, Amersfoort, The Netherlands **A double blind comparison of viloxazine and amitriptyline in involutional and endogenous depression.** Acta Psychiatrica Belgica. 79(2):198-209, 1979.

Thirty-two hospitalized patients with either endogenous or involutional depression were entered into a double-blind study to compare the effectiveness and acceptability of viloxazine with amitriptyline. The severity of the depression was assessed before starting treatment and at day 7, 14, and 28 using the Hamilton Rating Scale. Spontaneously reported side-effects were recorded. Viloxazine and amitriptyline were equally effective in endogenous depression, but viloxazine was significantly more effective than amitriptyline in patients with involutional depression. Nausea and vomiting were the main side-effects of viloxazine during early treatment necessitating the withdrawal of two patients. Anticholinergic side-effects were reported during amitriptyline treatment, but were absent in patients on viloxazine. It is concluded that viloxazine is an effective antidepressant and particularly useful in the treatment of involutional depression. 14 references. (Journal abstract modified)

**003541** Burrows, Graham D. Dept. of Psychiatry, University of Melbourne, Clinical Sciences Building, Royal Melbourne Hospital, Melbourne 3050, Australia **Which antidepressant?** Current Therapeutics. 20(2):83-85, 87-88, 1979.

A therapeutic guide to the treatment of depression is presented. A practical approach is based on the severity of the illness. Each antidepressant pharmacotherapy method is discussed in terms of response, dosage, and side-effects. If in doubt as to whether the patient suffers anxiety or depression, the more serious condition, depression, should prevail as far as therapy is concerned. A small number of nonresponders to tricyclics may respond to monoamine oxidase inhibitors. Lithium is best reserved for severe recurrent bipolar illnesses. It is concluded that concurrent psychotherapy in all types of depression is essential.

**003542** Coppen, A.; Rama Rao, V. A.; Ruthven, C. R. J.; Goodwin, B. L.; Sandler, M. MRC Neuropsychiatry Laboratory, West Park Hospital, Epsom, KT19 8PB Surrey, England **Urinary 4-hydroxy-3-methoxyphenylglycol is not a predictor for clinical response to amitriptyline in depressive illness.** Psychopharmacology. 64(1):95-97, 1979.

In an examination of 4-hydroxy-3-methoxyphenylglycol (HMPG) in urine as a predictor of clinical response, the urinary HMPG excretion of 23 unipolar depressives before and after treatment with amitriptyline was compared with urinary HMPG excretion in 27 age matched controls. There was no difference between patients and controls, although control females excreted less HMPG than males. After 6 weeks' treatment with 150mg daily of amitriptyline, there was no correlation between therapeutic response and pretreatment urinary excretion value. Thus, previously reported correlations between low HMPG values and depression and/or poor clinical response to amitriptyline could not be validated. Results also failed to provide support for the noradrenaline hypothesis of depressive illness. 22 references. (Author abstract modified)

**003543** Coppen, A.; Rama Rao, V.A.; Swade, Cynthia; Wood, K. MRC Neuropsychiatry Laboratory, West Park Hospital, Epsom KT19 8PB, Surrey, England **Inhibition of 5-hydroxytryptamine reuptake by amitriptyline and zimelidine and its relationship to their therapeutic action.** Psychopharmacology. 63(2):125-129, 1979.

The relationship between 5-HT uptake inhibition by tricyclic antidepressants and therapeutic outcome was investigated in depressed patients. Amitriptyline and zimelidine significantly re-

duced the uptake of 5-HT into the blood platelets of depressive patients. The degree of inhibition was significantly correlated with the plasma drug level of amitriptyline. No significant relationship could be detected between the degree of inhibition of uptake and therapeutic outcome. The accepted mode of action of tricyclic antidepressant drugs and the deficiency hypotheses of affective disorders are discussed. 22 references. (Author abstract)

**003544** Coppen, Alec; Swade, Cynthia; Wood, Keith. Medical Research Council Neuropsychiatry Lab., West Park Hospital, Epsom, KT19 8PB, Surrey, England **Lithium restores abnormal platelet 5-HT transport in patients with affective disorders.** British Journal of Psychiatry. 136(March):235-238, 1980.

m The effect of lithium on the kinetic variates of 5-hydroxytryptamine (5-HT) platelet accumulation in patients with affective disorder was investigated, as well as the effect of lithium on 5-HT platelet transport in vitro. Kinetic analysis of the transport of 5-HT into the blood platelets of 26 depressed patients and 25 recovered depressives showed that the rate of accumulation of 5-HT is significantly decreased both before and after recovery from the illness. A study of 35 patients receiving prophylactic lithium therapy showed that this abnormality is corrected by both short-term and long-term lithium treatment. The effect of lithium in vitro on 5-HT uptake was opposite to that reported in vivo. These findings suggest that lithium acts indirectly. Possible mechanisms of action are discussed. 13 references. (Author abstract modified)

**003545** Coryell, William; Ziegler, Vincent E.; Biggs, John T. Dept. of Psychiatry, University of Iowa College of Medicine, 500 Newton Road, Iowa City, IA 52242 **Symptoms as predictors of response to amitriptyline and nortriptyline.** Journal of Affective Disorders. 2(1):27-35, 1980.

Data collected to define therapeutic plasma levels of amitriptyline and nortriptyline were reanalyzed to test endogenous and nonendogenous symptoms as response predictors while controlling for plasma level variable. The selection criteria limited the range of historical predictors. Initial symptom quality was not predictive of outcome for the entire group of 44 patients or for the 27 with therapeutic plasma levels. Delusions were not associated with poor outcome. It is concluded that historical components of the endogenous/nonendogenous distinction (e.g., premorbid personality, stability of symptoms over time, quality of remissions) may be more important as response predictors. 24 references. (Author abstract)

**003546** Dunner, David L.; Murphy, Daniel; Stallone, Frank; Fieve, Ronald R. ZA-31 Harborview Medical Center, 325 Ninth Avenue, Seattle, WA 98104 **Episode frequency prior to lithium-treatment in bipolar manic-depressive patients.** Comprehensive Psychiatry. 20(6):511-515, 1979.

The true course of bipolar manic-depressive illness was investigated by retrospective study of episodes that occurred before the use of lithium-carbonate therapy to determine what factors are associated with episode frequency. Patients followed without lithium-were found to have failure rates of about 5% per month. In comparison, Bipolar-1 patients treated with lithium-have a failure rate of about 1% per month. Rehospitalization for relapses is rare with lithium-treatment as compared to the rehospitalization rate determined retrospectively. It is concluded that relapse rate in Bipolar-1 illness is not a function of age of onset but may be related to sex of patients. Recommendations for determinimg need for treatment with lithium-are offered. 12 references.

**003547** Ehrlich, Barbara Ellen. University of California, Los Angeles **The ups and downs of lithium. (Ph.D. dissertation).** Dissertation Abstracts International. 40(7):3019-B, 1980. Ann Arbor, Univ. Microfilms No. 8001368, 179p., 1979.

Membrane transport of lithium (Li) and Li's effect on membrane transport were investigated. It was found that RBC Li levels are maintained mainly by the balance of Li leak influx and Na-Li countertransport efflux. The RBC is a useful model for studying Li's effect on other cell membranes. The maximum rate of Li transport and the presence or absence of Li treatment are factors that determine interindividual differences in cell Li concentration. Li treatment alters choline transport in a variety of cells. It is suggested that Li treatment causes a general increase in cellular Li and choline levels analogous to the increase measured in RBC. In addition, it is suggested that alterations in choline and Li transport are an important aspect of Li's therapeutic action in treating mood disorders, since any of the Li-induced changes may lead to alterations in metabolic processes and/or cellular communication. (Journal abstract modified)

**003548** Friedman, Jeannette; Meares, Russell. University of Melbourne, Heidelberg, Victoria 3084, Australia **The effects of placebo and tricyclic antidepressants on cortical evoked potentials in depressed patients.** Biological Psychology. 8(4):291-302, 1979.

Cortical evoked potentials in depressives were recorded in order to study stimulus intensity control in this group, and also to study the effect of treatment. In a sample of 33 psychiatric patients, the amplitudes of visual and auditory evoked potentials were found to be significantly greater during depression than at recovery. The changes which appeared to be due to recovery were found not only in patients treated with tricyclic antidepressants (n=22), but also in those who had recovered following treatment with placebo (n=11). The changes were most evident in the auditory system. In addition, no diagnostic predictors differentiated depressed patients who subsequently recovered on placebo from those who did not. It is concluded that: 1) cortical evoked potentials may change in amplitude with emotional state and 2) placebo may have physiological consequences usually attributed to drugs alone. 36 references. (Author abstract)

**003549** Gastpar, M.; Hobi, V.; Poldinger, W.; Goldsmith, S.; Maly, V.; Schmidlin, P. E. Psychiatric University Clinic, CH-4025, Basel, Switzerland **A placebo-controlled comparative study of the combined effects of oxprenolol and clomipramine in depressed patients.** International Pharmacopsychiatry. 15(1):24-58, 1980.

In a double-blind study conducted in two different psychiatric units, the effects of standard therapy with clomipramine combined with oxprenolol were compared with those of clomipramine and placebo in 60 patients suffering from depression. The aim of the study was to ascertain whether concomitant medication with the beta-blocker had any measurably greater effect on depression and anxiety than treatment with clomipramine alone. The results showed that the more pronounced the symptoms were at the beginning of treatment the more linear or homogenous was the trend towards improvement. When the initial symptom scores were moderate, discrete differences between the two treatments were detectable; a more marked improvement being noted in response to clomipramine and oxprenolol than to clomipramine and placebo. The influence of the combination with oxprenolol also had a discretely more favorable influence on items relating to anxiety. The methodological problems associated with discriminative assessments of the two dimensions, anexity and depression, are discussed. It is concluded that the combined therapy with oxprenolol and clomipramine provided clinically effective and was very well tolerated by the patients. 37 references. (Author abstract modified)

**003550** Gelenberg, Alan J.; Wojcik, Joanne Doller; Growdon, John H.; Sved, Alan F.; Wurtman, Richard J. Dept. of Psychiatry, Massachusetts General Hospital, Boston, MA 02114 **Tyrosine for the treatment of depression.** American Journal of Psychiatry. 137(5):622-623, 1980.

A double-blind, placebo controlled, crossover trial of tyrosine in a depressed woman is described. Tyrosine, 100mg/kg, was administered for 2 weeks, a placebo for 18 days, and finally tyrosine for an additional 5 weeks. Evaluation was done by a psychiatrist and the subject; both were unaware of the change in medication. Both evaluations indicated complete alleviation of symptoms at the end of 2 weeks. By the end of the placebo period her depressive indices were slightly worse than pretreatment. These symptoms were again completely alleviated by the end of the trial with tyrosine. No adverse effects were noted. It is concluded that if tyrosine is demonstrated to be effective with a significant number of patients, and if it actually has few unwanted effects, it might become an attractive alternative to the antidepressants currently available. 10 references.

**003551** Giller, Earl, Jr.; Jatlow, Peter; Bialos, Donald; Harkness, Laurie; Docherty, John P. Psychiatry Service, 116A, V.A. Medical Center, West Spring Street, West Haven, CT 06516 **Platelet MAO and amitriptyline treatment.** Psychiatry Research. 2(3):259-265, 1980.

The effect on platelet monoamine oxidase (MAO) of stopping chronic amitriptyline treatment was investigated. Platelet MAO activity and drug levels were measured in depressed patients chronically being treated with amitriptyline and again 2 and 4 weeks after stopping the medication. Although tricyclic drug concentrations were initially within the therapeutic range and undetectable on placebo treatment, platelet MAO activities were unchanged. While three laboratories have clearly shown that tricyclic antidepressants inhibit MAO activity, predominantly activity of MAO B, the physiologic significance of this inhibition is unclear. It is suggested that reported alterations in platelet MAO activity with tricyclics may be secondary to other physiologic changes in patients recovering from depression instead of reflecting a direct chemical inhibition of the enzyme. 23 references. (Author abstract modified)

**003552** Hill, S. E.; Jenner, F. A.; Lee, C. R.; Paschalis, C.; Pollitt, R. J.; Sampson, G. A. University Dept. of Psychiatry, Middlewood Hospital, P.O. Box 134, Sheffield, S6 1TP, England **Urinary dicarboxylic acids in patients receiving lithium or rubidium salts.** Psychopharmacology. 65(1):85-87, 1979.

Lithium salts administered in therapeutic doses to four subjects who were kept on controlled diets are reported to have increased up to fivefold the urinary output of some dicarboxylic acids. Some of the acids affected are intermediates in the tricarboxylic acid cycle, others are chemically similar but not directly related in metabolic terms. This is probably a direct effect on renal transport. Rubidium salts increased urinary 2-oxoglutarate output and blood 2-oxoglutarate levels, probably by some action on intermediary metabolism. 15 references. (Author abstract)

**003553** Hollister, Leo E.; Pfefferbaum, Adolf; Davis, Kenneth L. Veterans Administration Hospital, 3801 Miranda Ave., Palo Alto, CA 94304 **Monitoring nortriptyline plasma concentrations.** American Journal of Psychiatry. 137(4):485-486, 1980.

Nortriptyline plasma concentrations and their effect on the outcome of treatment were examined in 20 depressed outpatients. Results indicate that monitoring plasma concentrations of nortriptyline did not increase the amount of time that patients spent at therapeutic plasma concentrations during treatment. The availability of such information did not affect the outcome of the patients. Feedback of plasma concentrations of drug to the treating physician tended to produce lower levels than were obtained when the drug was prescribed solely on the basis of clinical criteria of improving symptoms and tolerable side-effects. It is concluded that plasma concentrations of nortriptyline had little relationship to clinical outcome. 6 references.

**003554** Judd, Lewis L.; Janowsky, David S.; Segal, David S.; Huey, Leighton Y. Dept. of Psychiatry, M-003, School of Medicine, University of California at San Diego, La Jolla, CA 92093 **Naloxone-induced behavioral and physiological effects in normal and manic subjects.** Archives of General Psychiatry. 37(5):583-586, 1980.

The effects of intravenous naloxone hydrochloride (20mg) were investigated with eight normal control Ss and 12 affective disorder patients manifesting manic or hypomanic symptoms. On two consecutive days, in a counterbalanced order, naloxone and placebo were given in a double-blind cross-over design. The overall effect of naloxone was to decrease pulse rate and to promote lethargy and inactivation. Controls manifested reduced feelings of well-being, and the manic patients noted a subjective sense of slowing, with four of the 12 patients showing an observable reduction in manic symptoms and behavior after the naloxone administration. Naloxone seems to have a nonspecific subduing effect in both normal Ss and patients and may also have a selectively greater effect on a small subsample of manics. 22 references. (Author abstract modified)

**003555** Kammerer, Th.; Zupnik, S. no address **/The benefit of a single 75mg dose of maprotiline given at bedtime./** Interet de la maprotiline (1) 75mg administree en une seule prise vesperale./ Annales Medico-Psychologiques. 137(6-7):578-583, 1979.

The effect of maprotiline, an antidepressant manufactured under the name of Ludiomil Ciba-Geigy, was tested on 40 hospitalized patients, 26 females and 14 males. It was found highly effective against inhibition, agitation, anxiety, hypochondria, and insomia. The therapeutic effectiveness of a single pill of 75mg taken at 17:00 hours was the same as that of the average of 2 to 3 pills of 25mg per day. In 10 cases, the dose was found insufficient and was doubled. It is concluded that the use of one single 75mg pill has the advantage of reducing administration of the pill to one in 24 hours. Maprotiline has a sedative effect and induces sleep in about one third of the patients. A discussion follows the text of the article.

**003556** Kaneko, Motohisa; Kumashiro, Hisashi; Takahashi, Yukio; Hoshino, Yoshihiko. Dept. of Neuropsychiatry, Fukushima Medical College, Sugitsuma-cho 4-45, Fukushima-shi, Fukushima-ken, Japan **L-5-HTP treatment and serum 5-HT level after L-5-HTP loading on depressed patients.** Neuropsychobiology. 5(4):232-240, 1979.

The therapeutic effect of L-5-hydroxytryptophan (L-5-HTP) on endogenous depression and its relationship to serum 5-HT level was investigated with 18 depressed patients. The global estimates were two very much improved; eight much improved; three minimally improved, and five unchanged. The action of L-5-HTP was usually rapid. The elevation of the serum 5-HT level 1 week after L-5-HTP administration was relatively lower in the 5-HTP nonresponder group, compared with responders. The chronological change of the serum 5-HT level in depressed patients after an oral loading dose of 3mg/kg of L-5-HTP showed a gradual and slight elevation, compared with manic and normal groups. It is suggested that the therapeutic effect of L-5-HTP on responders is related to lower 5-HT level in the brain for their pathogenesis, and that there is a metabolic disturbance of L-5-HTP into 5-HT in some depressed patients. 30 references. (Author abstract modified)

**003557** Kaskey, Gary B.; Nasr, Suhayl; Meltzer, Herbert Y. Meltzer: Dept. of Psychiatry, University of Chicago, Pritzker School of Medicine, 950 E. 59th Street, Chicago, IL 60637 **Drug treatment in delusional depression.** Psychiatry Research. 2(3):267-277, 1980.

In a retrospective study, the drug response of delusional patients with primary depression who were treated with tricyclic antidepressants (TCA), neuroleptics, or combined TCA plus neuroleptic therapy was examined. Significantly more patients responded to the combined drug regimen, as has been found in other recent studies. Clinical response was not related to severity of symptoms, drug dosage, or demographic characteristics. The clinical superiority of neuroleptics plus TCA in the treatment of delusionally depressed patients suggests the possible role of dopamine in the psychosis associated with depression and implicates norepinephrine and serotonin in the disordered locomotor activity and mood of primary depressive illness. 23 references. (Author abstract)

**003558** Kellner, R.; Rada, R. T.; Andersen, T.; Pathak, Dorothy. Dept. of Psychiatry, University of New Mexico School of Medicine, Albuquerque, NM 87131 **The effects of chlordiazepoxide on self-rated depression, anxiety, and well-being.** Psychopharmacology. 64(2):185-191, 1979.

The effects of chlordiazepoxide (CDP) on self-rated depression, anxiety, and well-being was examined in 22 anxious and depressed nonpsychotic psychiatric outpatients using a double-blind crossover design. All self-ratings of depression, anxiety, somatic symptoms, and feelings of inadequacy discriminated significantly between CDP and placebo. The decrease in self-rated depression was about equal to the decrease in self-rated anxiety. Subscales describing well-being were more sensitive to drug effects than subscales describing symptoms. A questionnaire (the Symptom Questionnaire) and one of the self-rating scales (Symptom Rating Test) were more sensitive than global self-rating scales, global observer rating scales, and the Hamilton Anxiety Rating Scale. Some of the self-rating scales discriminated significantly between drug and placebo even when sample size was reduced to two subsamples of eight patients each. High and significant positive correlations between the two scales did not indicate equal sensitivity in discriminating between drug and placebo. 23 references. (Author abstract modified)

**003559** Kiloh, L. G.; Bartrop, R. W.; Franklin, Janet A.; Neilson, Megan D. Dept. of Psychiatry, University of New South Wales, New South Wales, Australia **A double blind comparative trial of viloxazine and amitriptyline in patients suffering from endogenous depression.** Australian and New Zealand Journal of Psychiatry. 13(4):357-360, 1979.

A double-blind trial was conducted comparing viloxazine and amitriptyline in 12 outpatients and 35 inpatients suffering from endogenous depression. Of these, six failed to complete the trial: two because of severity of illness; and four on viloxazine because of nausea during the first treatment week, who refused to continue in treatment. Clinical status was evaluated at initiation of treatment and every 7 days thereafter during the 28 day trial period. An overall response rate of 51% was found, and results indicated that viloxazine is similar in effectiveness to amitriptyline. There were no differences between the two drugs in time taken for improvements to occur. Although side-effects were frequent, apart from nausea and vomiting, these appeared to be less marked for viloxazine than with amitriptyline. 14 references.

**003560** Kuhne, G.-E.; Beier, R.; Heim, M.; Knorr, W.; Perina, L.; Richter, H.; Rossberg, V.; Sorger, R.; Waldow, N. Nervenklinik der Medizinischen Akademie Magdeburg, Leipziger Strasse 44, DDR-301, Magdeburg, Germany /**The differential indication for trimipramine -- results of a controlled multiclinical study./** Zur differentialindikation von trimipramin -- Ergebnisse einer kontrollierten multiklinischen Studie. Psychiatrie Neurologie und Medizinische Psychologie. 31(4);203-212, 1979.

The antidepressants trimipramine and imipramine were compared within the framework of a multiclinical study performed under the conditions of a controlled clinical experiment. A time different remission of affective and psychosomatic symptoms was found. The panthymoleptic action of trimipramine and other antidepressants is discussed with reference to these results. Trimipramine influences psychotic states, especially if depressive anxiety is combined with agitation or in hypochondriac forms of depression. 21 references. (Journal abstract)

**003561** Kupfer, David J.; Spiker, Duane G.; Coble, Patricia A.; Neil, John F.; Ulrich, Richard; Shaw, David H. Western Psychiatric Institute and Clinic, 3811 Otlara Street, Pittsburgh, PA 15261 **Depression, EEG sleep, and clinical response.** Comprehensive Psychiatry. 21(3):212-220, 1980.

The relationship between EEG sleep and clinical drug response was examined in 30 primary depressive inpatients treated with amitriptyline during an intensive 35 day protocol involving ongoing clinical assessment and nightly EEG studies. Baseline sleep characteristics of subjects under went immediate and major changes within the first two nights of drug administration. Replicating and extending previous findings, drug effects, notably REM suppressions, on the first two nights were predictive of clinical change occuring 3 to 4 weeks later. With regard to changes in sleep latency, some patients did not experience a sedative effect of the first two nights: this paradoxical alerting effect of amtriptyline in certain patients mav help identify a subgroup of tricyclic nonresponders, and was in fact the strongest covariate effect found. 23 references.

**003562** Laux, G.; Reimer, F. Psychiatrisches Landeskrankenhaus, D-7102 Weinsberg, Germany /**Treatment of therapy resistant depressions with high dosage infusions of clomipramine./** Behandlung therapieresistenter Depressionen mit hochdosierten Clomipramin-Infusionen. International Pharmacopsychiatry. 14(5):294-299, 1979.

The efficacy of high dosage intravenous clomipramine infusions was investigated in 50 therapy resistant depressed inpatients using a fixed therapy schedule with increasing and decreasing doses ranging from 250 to 500mg. The majority of the inpatients showed sufficient or good therapeutic effects; notable side-effects were rare. The therapeutic possibilities in therapy resistant depressions are discussed. 16 references. (Journal abstract modified)

**003563** Lecrubier, Y.; Puech, A. J.; Jouvent, R.; Simon, P.; Widlocher, D. Department de Psychiatrie Adulte, Hopital de la Salpetriere, 47 Boulevard de l'Hopital, F-75013 Paris, France **A beta adrenergic stimulant (salbutamol) versus clomipramine in depression: a controlled study.** British Journal of Psychiatry. 136(April):354-358, 1980.

The comparative effects of salbutamol (6mg/day) and clomipramine (150mg/day) were studied with depressed patients under controlled conditions. The symptomatology was evaluated by two blind observers at days 1, 5, and 15 using the Hamilton Rating Scale. Both treatments were found to be effective on the overall symptomatology but the onset of action of salbutamol was more rapid. 8 references. (Author abstract modified)

**003564** Mallinger, A. G.; Mallinger, J.; Himmelhoch, J. M.; Neil, J. F.; Hanin, I. Western Psychiatric Institute and Clinic, 3811 O'Hara St., Pittsburgh, PA 15261 **Transmembrane distribu-**

**tion of lithium and sodium in erythrocytes of depressed patients.** Psychopharmacology. 68(3):249-255, 1980.

The correlation between in vitro and in vivo measures of the intracellular/extracellular distribution of lithium across the erythrocyte membrane was abolished by the addition of ouabain to the in vitro incubation media. In vitro studies of erythrocytes from depressed patients and nondepressed controls indicated that lithium transport characteristics may be different in bipolar patients than in other depressed patients and nondepressed Ss. After in vitro incubation with lithium for 48 hours, erythrocytes from bipolar depressed patients had lithium distribution values similar to those observed in ouabain treated cells. 61 references. (Author abstract modified)

**003565** Marneros, Andreas; Philipp, M. Universitats-Nervenklinik, Josef-Stelzmann-Strasse 9, D-5000 Cologne 41, Germany **A double-blind trial with amitriptyline and lofepramine in the treatment of endogenous depression.** International Pharmacopsychiatry. 14(5):300-304, 1979.

A double-blind trial was undertaken to compare the antidepressive efficacy and the side-effects of lofepramine with those of amitriptyline in the treatment of endogenous depression. The study involved 22 acutely ill endogenously depressive patients; 11 treated with lofepramine and the remaining 11 treated with amitriptyline. Both substances were found to be effective in the treatment of depression. However, the therapeutic efficacy of lofepramine was significantly greater than that of amitriptyline. Futhermore, the tolerance of lofepramine was significantly better than that of amitriptyline; and the side-effects of amitriptyline, especially in blood pressure dysregulation, were greater than those of lofepramine. 4 references. (Author abstract)

**003566** Mielke, D. H.; Koepke, R. P.; Phillips, J. H. Tulane University Medical Center, New Orleans, LA 70112 **Controlled evaluation of tetracyclic (maprotiline) and tricyclic (imipramine) antidepressant and their effects on heart.** Current Therapeutic Research. 25:738-743, 1979.

Fifty-two patients with symptomatic depression were treated with either a tetracyclic (maprotiline) or a tricyclic (imipramine) antidepressant in a double-blind, randomized, flexible dose design. The Zung Self-Rating Scale and the Hamilton Rating Scale for Depression showed significant and equivalent improvement in both groups while the Psychiatrist's Global Evaluation of Improvement showed a better response in the imipramine group. Significant changes in both groups during treatment included a decrease in the standing systolic blood pressure, an increase in both the standing and supine pulse rates, and a lengthening of the corrected QT interval. These changes were equivalent in both groups. Electrocardiogram, echocardiogram, and treadmill stress tests showed no significant change. (Journal abstract modified)

**003567** Minter, Richard E.; Verdugo, Nancy; Mandel, Michel R. Dept. of Psychiatry, University of Michigan Medical Center, 1405 East Ann Street, Ann Arbor, MI 48109 **The treatment of delusional depression with tranylcypromine: a case report.** Journal of Clinical Psychiatry. 41(5):178, 1980.

The case is reported of a patient with tricyclic intolerant, delusional depression who failed to respond to electroconvulsive therapy (ECT) and haloperidol but who subsequently responded well to tranylcypromine. The patient was given tranylcypromine, 20mg daily for 3 weeks and then 30mg daily. After 5 to 7 days on the higher dose, she experienced dramatic relief of phobic anxiety, disappearnace of delusions, and remission of all depressive symptoms except for persistence of mild depressed mood and mild insomnia. At 6 months followup, she had remained well and was being maintained on tranylcypromine, 20mg per day with no ill effects. The good response shown by this patient suggests that tranylcypromine should be considered in cases of psychotic depression where phobias and anxiety are prominent features. 6 references.

**003568** Moller, S. E.; Kirk, L.; Honore, P. Research Laboratory C-D, Sct. Hans Mental Hospital, DK-4000 Roskilde, Denmark **Relationship between plasma ratio of tryptophan to competing amino acids and the response to L-tryptophan treatment in endogenously depressed patients.** Journal of Affective Disorders. 2(1):47-59, 1980.

The ratio in the plasma of total tryptophan to those amino acids that compete with tryptophan during transport into the brain was determined in 60 control subjects and 87 patients suffering from endogenous depression, all females. The plasma ration in the control subjects showed a significant negative correlation with age. There was no significant difference in the distribution of the biochemical data between the control subjects and the depressed patients. There was a significant higher proportion of bipolar depressed subjects compared to unipolar depressives and patients of uncertain polarity who showed a plasma ratio in the lower normal range. Thirty-two patients were subsequently treated with L-tryptophan. In the patients who showed a particularly low plasma ratio of tryptophan to competing amino acids a remission frequency of 80% was observed on day 14. The efficacy of L-tryptophan in the patients who showed a plasma ratio within the upper normal range was extremely poor. The results suggest that the ratio in the plasma of tryptophan to competing amino acids is a useful predictor of the course of treatment of depressed subjects with L-tryptophan. 54 references. (Author abstract)

**003569** Odejide, A. O. Dept. of Psychiatry, University of Ibadan, Ibadan, Nigeria **Patterns of psychotropic drug use in a Nigerian psychiatric outpatient clinic.** International Pharmacopsychiatry. 15(1):14-23, 1980.

The prescription pattern of clinicians in a Nigerian psychiatric outpatient clinic was studied. The three major psychiatric disorders diagnosed at the center were schizophrenia, affective disorders, and psychoses associated with other cerebral conditions. The schizophrenics were treated essentially with neuroleptics in different combinations. Also, combinations of neuroleptics and antidepressants were employed in the few cases diagnosed as schizoaffective disorders. As for the cases of affective disorders, a combination of neuroleptics and antidepressants was found to be the pattern. The reasons for this pattern of treatment were discussed. The average maintenance neuroleptic dose per day was 300mg while those of the tricyclic antidepressants was 88mg. In as much as psychopharmacotherapy is widely employed in treating the various psychiatric disorders in African countries, especially Nigeria, the need for more information on psychotropic drugs through training courses suggested. 14 references. (Author abstract)

**003570** Okuma, Teruo; Inanaga, Kazutoyo; Otsuki, Saburo; Sarai, Keisuke; Takahashi, Ryo; Hazama, Hidefumi; Watanabe, Masasuke. Dept. of Psychiatry, Tohoku University School of Medicine, 1-1, Seiryo-machi, Sendai, Japan **Comparison of the antimanic efficacy of carbamazepine and chlorpromazine: a double-blind controlled study.** Psychopharmacology. 66(3):211-217, 1979.

Carbamazepine (Tegretol) was compared with chlorpromazine in a controlled, double-blind study in 63 cases of endogenous manic psychosis to evaluate carbamazepine's clinical utility and efficacy. The overall improvement rate, based on the number of cases showing moderate to marked amelioration of

manic symptoms, was 70% in the carbamazepine group and 60% in the chlorpromazine group. No significant differences were found between the two groups. Improvements in basic mood, insomnia, headache, lassitude, and diurnal fluctuations of mood tended to be characteristic of carbamazepine efficacy for mania compared with the effects of chlorpromazine. It is suggested that carbamazepine is potentially useful for the treatment of the manic state. 18 references. (Author abstract modified)

**003571** Peet, Malcolm; Coppen, Alec. Coppen: West Park Hospital, Epsom, Surrey, England **Lithium treatment and prophylaxis in unipolar depression.** Psychosomatics. 21(4):303, 304, 306-309, 313, 1980.

The evidence regarding the therapeutic value of lithium in both the prophylaxis of recurrent unipolar depression and the treatment of the acute depressive episode is examined. It is found that as a treatment for acute unipolar depression it is less effective than the standard antidepressant drugs or electroconvulsive therapy. However, a therapeutic trial of lithium may be indicated in acutely depressed patients who fail to respond to conventional treatment. Recommendations as to whom to give lithium to, when to start it, and when to stop it are made. 41 references. (Author abstract modified)

**003572** Potter, William Z.; Calil, Helena M.; Extein, Irl; Zavadil, Anthony P., III; Goodwin, Frederick K. Clinical Psychobiology Branch, NIMH, 9000 Rockville Pike, Bldg. 10, Rm. 4S239, Bethesda, MD 20205 **Comparative pharmacokinetics of zimelidine and desipramine in man following acute and chronic administration.** Psychiatry Research. 1(3):273-281, 1979.

Single dose and steady-state pharmacokinetics of zimelidine and desipramine were compared in eight depressed patients who were subjects in a double-blind crossover study. Within the same patient, there was no relationship between the pharmacokinetics of desipramine (pharmacokinetically similar to all other tricyclic antidepressants) and those of zimelidine, a bicyclic antidepressant. The weight corrected dose of zimelidine was found to give a reasonable index of the concentration of its active metabolite norzimelidine, which predominates over zimelidine by a ratio of approximately three to one. The variation in steady-state concentration of norzimelidine for a given dose of zimelidine in adults is reported to be about two fold and can be reduced by correcting for weight. 14 references. (Author abstract)

**003573** Prusoff, Brigitte Auerbach. Yale University **Predictors of response to amitriptyline, perphenazine, amitriptyline and perphenazine in three independent double-blind clinical trials with acutely depressed outpatients. (Ph.D. dissertation).** Dissertation Abstracts International. 40(1):164-B, 1979. Ann Arbor, Univ. Microfilms No. 7916518, 274p., 1978.

Three randomized short-term clinical trials were conducted on 485 depressed patients with mixed symptoms of anxiety and depression to investigate the efficacy of amitriptyline and perphenazine, alone or in combination. The clinical and social characteristics which distinguish response in these three medication groups were also studied. All drugs produced a substantial improvement of symptoms over 4 to 6 weeks of treatment. Overall there was no difference in the relative efficiency of the combination of drugs against the individual components. Neither symptoms ratings nor demographic variables showed a strong enough relationship with outcome to be clinically meaningful. (Journal abstract modified)

**003574** Reifler, Burton V.; Ward, Nicholas G. Dept. of Psychiatry RP-10, School of Medicine, University of Washington, Seattle, WA 98195 **A Comparison of the use of tricyclic antidepressants by psychiatrists and non-psychiatric physicians.** International Journal of Psychiatry in Medicine. 10(1):41-49, 1980.

The use of tricyclic antidepressants by psychiatrists and nonpsychiatric physicians was investigated via chart review of 25 psychiatry patients and 25 nonpsychiatry patients receiving tricyclic antidepressants. Results indicate that the psychiatrists performed significantly better in documenting a diagnosis of depression and in documenting length of treatment and continued need for patients already on a tricyclic antidepressant. In other areas (including route, frequency of administration, and use of multiple psychoactive drugs) there were no differences between the two groups. It is concluded that performance by psychiatrists is better than for nonpsychiatrists but below what might be set as reasonable standards, particularly in the area of documenting specific signs and symptoms of depression in patients receiving tricyclic antidepressants. 13 references. (Author abstract modified)

**003575** Rey, Alix C.; Jimerson, David C.; Post, Robert M. Post: NIH, 9000 Rockville Pike, Building 10, Room 3S239, Bethesda, MD 20205 **Lithium and electrolytes in cerebrospinal fluid of affectively ill patients during acute and chronic lithium treatment.** Communications in Psychopharmacology. 3(4):267-278, 1979.

Cerebrospinal fluid (CSF) and serum concentrations of lithium and electrolytes were assessed acutely and chronically in 10 patients with primary affective disorders. Lithium carbonate was administered in a double-blind trial at doses of 1200 to 1500mg/day to achieve serum levels between 0.60 and 1.20 mEq/l. Lumbar punctures (LP) were performed in the baseline period (2 weeks free of medication) and during lithium administration acutely (6 to 10 days), chronically (3 to 4 weeks) or after an extended clinical trial (6 weeks or greater). The data indicate that at commonly accepted therapeutic oral doses, CSF lithium levels were 0.20 mEq/l acutely and with chronic treatment the levels increased to 0.32 mEq/l. The CSF/serum lithium ratios were 0.30 acutely and 0.35 during chronic lithium treatment. CSF calcium and magnesium decreased significantly during acute, but not chronic lithium administration. The several week lag before final CSF and serum lithium levels are achieved using standard, nonloading dose treatment might partially explain the usual delay in onset of clinical efficacy of lithium carbonate in affective illness. 37 references. (Author abstract)

**003576** Rifkin, Arthur; Saraf, Kishore; Kane, John; Ross, Donald; Klein, Donald F. Dept. of Psychiatry, Mount Sinai School of Medicine, One Gustave L. Levy Place, New York, NY 10029 **A comparison of trimipramine and imipramine: a controlled study.** Journal of Clinical Psychiatry. 41(4):124-129, 1980.

Trimipramine, a new tricyclic antidepressant, was compared to imipramine in the treatment of 38 hospitalized depressive patients. Both trimipramine and imipramine groups improved, with no major differences between the drugs. Analysis of the power of the statistical analysis shows that it is very unlikely that a true difference was present and remained undetected. Fewer adverse reactions to trimipramine were reported than to imipramine. Measures employed include: the Clinical Global Impression Scale; Zung Self-Rating Depression Scale; Hamilton Rating Scale for Depression; Brief Psychiatric Rating Scale; Nurses' Observation Scale for In-Patient Evaluation; and Treatment Emergent Symptoms. 8 references. (Author abstract modified)

**003577** Sachar, Edward J.; Asnis, Gregory; Nathan, Swami; Halbreich, Uriel; Tabrizi, Mary Ann; Halpern, Frieda S. Dept. of Psychiatry, College of Physicians and Surgeons, Columbia University, 722 W. 168th St., New York, NY 10032 **Dextroamphetamine and cortisol in depression: morning plasma cortisol levels suppressed.** Archives of General Psychiatry. 37(7):755-757, 1980.

Dextroamphetamine sulfate was administered intravenously in the morning to 11 unmedicated depressed patients and suppressed previously elevated plasma cortisol levels to normal in 90 minutes. Ten other depressed patients, without amphetamine, maintained high cortisol levels during the same time period. In each of five normal young men, amphetamine identically administered stimulated a rise in cortisol between 15 and 30 minutes after infusion; by 90 minutes after amphetamine administration plasma cortisol had fallen to normal and identical levels in both groups. Since noradrenalin normally inhibits hypothalamic corticotropin releasing factor (and adrenocorticotropic hormone) secretion, it is suggested that a noradrenergic deficit may account for cortisol hypersecretion in depression and that amphetamine may transiently correct this deficit in depressed patients, thereby reducing their cortisol secretion. 19 references. (Author abstract)

**003578** Sitaram, N.; Nurnberger, John I., Jr.; Gershon, Elliot S.; Gillin, J. Christian. Biological Psychiatry Branch, National Institute of Mental Health, Bethesda, MD 20205 **Faster cholinergic REM sleep induction in euthymic patients with primary affective illness.** Science. 208(4440):200-202, 1980.

The speed with which REM sleep is induced by arecoline, a cholinergic muscarinic agonist, was compared for 21 patients with primary affective illness in remission and 16 normal controls. Arecoline was found to induce REM sleep significantly more rapidly in patients with primary affective illness in remission than in controls. The cholinergic REM induction response per se was not significantly correlated in any subject group with age, sex, weight, or sleep EEG measures. These results, as well as those of other studies, suggest that patients with primary affective illness may have a supersensitive cholinergic system both when they are ill and when their symptoms are in clinical remission. 23 references. (Author abstract modified)

**003579** Szentistvanyi, I.; Janka, Z.; Szilard, J. Dept. of Neurology and Psychiatry, University Medical School, Szeged, Hungary **Clinical significance of sodium-dependent lithium transport in affective psychoses.** Psychiatria clinica. 13(1):57-64, 1980.

The steady-state red blood cell/plasma lithium (Li) ratios were determined simultaneously with the in vitro rates of sodium dependent Li transport of erythrocytes during prophylactic Li therapy in 30 unipolar and 52 bipolar forms of manic-depressive patients, and in 58 nonmanic-depressive psychiatric patients as a control group. A reciprocal correlation was found between the Li ratios and the values of sodium dependent Li transport. These transport rates were in positive correlation with the steady-state Li contents of red blood cells and that of the plasma. Significant differences were revealed between the different nosologic subgroups in the respect of in vitro rates of sodium dependent Li countertransport. Results are discussed from clinical and pharmacogenetic points of view. 34 references. (Author abstract)

**003580** van Hiele, L. J. Outpatient Dept., Mental Hospital, Franeker, The Netherlands **l-5-Hydroxytryptophan in depression: the first substitution therapy in psychiatry? The treatment of 99 out-patients with** Neuropsychobiology. 6(4):230-240, 1980.

The efficacy of l-5-hydroxytryptophan (5-HTP) in combination with the peripheral decarboxylase inhibitor, carbidopa, which prevents 5-HTP from being converted to serotonin (5-HTP) before it passes the blood/CSF barrier, was examined in 99 therapy resistant depressive outpatients. Subjects ijcluded patients with chronic depression, recurrent unipolar and bipolar depressions, and chronic depressions with recurrent exacerbations. This treatment produced complete recovery in 43 and evident recovery in 8 of these patients without side-effects. In patients for whom 5-HTP was effective recovery was rapid and complete. This apparent all or none effect provides support for van Praag's hypothesis on the biochemical typology of depressions: 25 of 44 vital depressions and 18 of 24 depressions with vital features showed improvement, while improvement was found in only 8 of 31 personal depressions. 25 references. (Author abstract modified)

**003581** Ward, Nicholas G.; Bloom, Valerie L.; Friedel, Robert O. Dept. of Psychiatry and Behavioral Sciences, RP-10, University of Washington, Seattle, WA 98195 **The effectiveness of tricyclic antidepressants in the treatment of coexisting pain and depression.** Pain. 7(3):331-341, 1979.

The frequency and nature of pain complaints and their response to doxepin were examined with a group of moderately to severely depressed individuals with moderate anxiety. It was discovered that 100% of these subjects had chronic pain complaints, most of which paralleled the course of depression. Headache was most commonly noted. Doxepin's analgesic effects were intimately associated with its antidepressant effects. It is concluded that there is a highly significant relationship between improvement of depression and reduction of pain on doxepin. 33 references. (Author abstract modified)

**003582** Weise, Charles C.; Stein, Marsha K.; Pereira-Ogan, Jorge; Csanalosi, Irma; Rickels, Karl. Rickels: Dept. of Psychiatry, Hospital of the University of Pennsylvania, 203 Piersol Bldg., 3400 Spruce St., Philadelphia, PA 19104 **Amitriptyline once daily vs three times daily in depressed outpatients.** Archives of General Psychiatry. 37(5):555-560, 1980.

Two dosage schedules of amitriptyline hydrochloride, once daily vs three times daily, were compared in a group of 124 nonpsychotic depressed outpatients. After 4 weeks of treatment, patients on the once daily schedule had improved significantly more than patients receiving multiple doses, on both physician and patient measures. The two groups did not differ in their attrition rates nor in reporting of side-effects. Since treatment response to the tricyclic antidepressants is often delayed, once daily dosage seems to offer a distinct advantage over more conventional multiple doses in depressed outpatients. 34 references. (Author abstract)

## 10 DRUG TRIALS IN NEUROSES

**003583** Ananth, J.; Pecknold, J. C.; Van Den Steen, N. Allan Memorial Institute, 1025 Pine Ave., West, Montreal, P.Q., Canada **Double-blind comparative study of chlorimipramine in obsessive neurosis.** Current Therapeutic Research. 25:703-709, 1979.

The therapeutic efficacy and safety of chlorimipramine was compared with that of amitriptyline in 20 obsessive compulsive neurotic patients in a 4 week double-blind clinical trial. Improvement in the total obsessive symptoms and severity scores was statistically significant only in the chlorimipramine group. Similarly, total depression as well as anxiety scores improved statistically significantly only in the chlorimipramine group while the total phobia score improved significantly in both groups. In the chlorimipramine group antiobsessive effect preceded antidepressant effect. Findings indicate that chlorimipramine is safe and effective, and its efficacy is greater than that of the standard drug amitriptyline; however, long-term efficacy needs to be proven. (Journal abstract modified)

**003584** Dasberg, Haim H.; Shalif, Ilan. Ezrath Nashim Hospital, P.O.B. 140, Jerusalem, Israel **Brief treatment with oxazepam in crisis intervention -- with a symptom-profile study in acute anxiety patients.** Israel Annals of Psychiatry and Related Disciplines. 17(3):201-208, 1979.

A nonmetric statistical description of drug specific multidimensional symptom profiles is developed and compared to a unidimensional approach. Twenty-two adult anxious neurotic patients completed a two week crisis intervention program. Treatment consisted of psychotherapeutic intervention combined with a daily dose of oxazepam. Pretreatment symptoms profiles codetermined outcome. Subjects responding to the anxiolytic effect of oxazepam had profiles high on free floating anxiety, acute obsessive symptoms, emotional lability, and somatic complaints. The depressant action of oxazepam became apparent in subjects with different symptoms: neurotic depressiveness and longstanding obsessive and phobic symptoms. It is concluded that the multidimensional scaling techniques demonstrate a finer sensitivity than traditional unidimensional techniques. 14 references. (Author abstract modified)

**003585** Goldberg, Harold L.; Finnerty, Richard J. West-Ros-Park Mental Health Center, 26 Central Avenue, Hyde Park, MA 02136 **Double-blind study of prochlorperazine, chlordiazepoxide and placebo in psychoneurotic outpatients with dominant symptoms of anxiety.** International Pharmacopsychiatry. 14(5):264-277, 1979.

A double-blind study of prochlorperazine, chlordiazepoxide, and placebo was conducted in 119 psychoneurotic outpatients with dominant symptoms of anxiety. Patients were accepted for the study when their pretreatment symptoms of anxiety met the criterion of a score of 21 or greater on the Hamilton Anxiety Rating Scale (HARS). The study interval was 4 weeks. The HARS, the New Physician Rating List, and Global Evaluation were used. Patients completed the Self-Rating Symptom Scale and the Profile of Mood States. All efficacy criteria ranked the study medications in the same order. Prochlorperazine was most effective. There were statistically significant active medication versus placebo comparisons supporting desirable drug action. Chlordiazepoxide versus placebo approached statistical significance for all efficacy criteria. (Author abstract modified)

**003586** Gottschalk, Louis A.; Kaplan, Stanley A. Dept. of Psychiatry and Human Behavior, College of Medicine, University California, Irvine, CA 92664 **Chlordiazepoxide plasma levels and clinical responses.** In: Gottschalk, L., The content analysis of verbal behavior. New York, SP Medical & Scientific Books, 1979. 977 p. (p. 415-423).

The effects on several psychological states of a single oral dose of chlordiazepoxide (25mg) on 18 chronically anxious Ss were investigated in a double-blind, cross-over study. Anxiety, hostility outward, and ambivalent hostility scores tended to decrease over the 50 minute observation period when subjects were on chlordiazepoxide as compared to placebo. However, this decrease did not reach significant levels. Data illustrate that a wide range of differences in chlordiazepoxide plasma levels occured in 18 anxious individuals receiving identical dosages of this pharmacological agent. Findings emphasize the importance of individual differences in drug metabolism and the bearing such differences can have on drug efficacy. 36 references.

**003587** Marks, I. M.; Stern, R. S.; Mawson, D.; Cobb, J.; McDonald, R. Institute of Psychiatry, London, England **Clomipramine and exposure for obsessive-compulsive rituals:** British Journal of Psychiatry. 136(Jan):1-25, 1980.

Forty chronic obsessive-compulsive ritualizers were randomly assigned to treatment with oral clomipramine or placebo for 8 months; at weeks 4 to 7 these two groups were randomly split into treatment by relaxation or by exposure in vivo, and during weeks 7 to 10 all patients had exposure in vivo. Clomipramine produced significant improvement in rituals, mood, and social adjustment, but only in those patients who initially had depressed mood. It is concluded that clomipramine is useful for compulsive ritualizers with depressed mood, but may need continuation for over a year and combination with exposure in vivo. Exposure in vivo is reported to remain the treatment of choice for ritualizers without depressed mood. 55 references. (Author abstract modified)

**003588** Scharbach, H. Service de Psychiatrie IV, Centre Hospitalier Regional, 85, rue Saint-Jacques, F-44035 Nantes, France / **Voluntary poisoning with beta-blocking agents.**/ Les intoxications volontaires par les substances beta-bloquantes. Therapie. 34(2):249-254, 1979.

A case of voluntary poisoning with propanolol, a beta blocking agent, is discussed. The beta blocking substances appear to have a reducing action on anxiety, especially when the anxiety is of a somatic nature, and are therefore prescribed for cardiovascular cases. The subject in this case ingested the propranolol with suicidal intent and remained depressed, adynamic, and asthenic for 6 months causing marital problems with her husband. The problem of intensive care in voluntary poisoning is serious, but the cardiovascular disturbances often appear less important than their specific activity would suggest, and they are relatively easily reduced. 19 references. (Journal abstract modified)

**003589** Sladka, R.; Dostalova, J.; Haskovcova, V.; Jarosova, M.; Faltus, F.; Slanska, J.; Filip, V. Division of Psychiatry, District Institute of National Health, Prague, Czechoslovakia **A placebo-controlled clinical trial with tofizopam in the treatment of anxiety neurosis.** Therapia Hungarica. 27(4):176-180, 1979.

The effectiveness of tofizopma, a benzodiazepine derivative, was evaluated in a clinical trial of patients with anxiety neuroses. Subjects were 25 male and 25 female psychiatric outpatients. In the male patients there was a significantly greater improvement with tofizopam than with placebo in somatic anxiety, tension, insomnia, somatic/sensory, cardiovascular symptom, geniro-urinary symptom, and anxiety scale scores. In the female subjects, tofizopam was more effective than placebo in fear scores on the Hamilton Anxiety Scale. The effects of tofizopam and placebo were equal in regard to daytime vigilance and intellectual performance. The reported adverse effects, hypertension and jerking calf muscles, were of uncertain relationship to the medication. 4 references. (Author abstract modified)

**003590** Zimmermann-Tansella, Christa; Tansella, Michele; Lader, Malcolm. Istituto di Clinica Psichiatrica di Verona, Policlinico, I-37134 Verona, Italy **Psychological performance in anxious patients treated with diazepam.** Progress in Neuro-Psychopharmacology. 3(4):361-368, 1979.

A comprehensive battery of clinical ratings, subjective tests, and psychological performance tasks was used to detect clinical and psychological effects of diazepam, amylobarbitone, and placebo in anxious patients. Self-rated anxiety and insomnia were both significantly improved by the diazepam treatment, but amylobarbitone improved only the insomnia. Impaired performance was detected on two performance tests following barbiturate treatment and on six performance tests after benzodiazepine treatment. The patient's reported level of anxiety under each treatment condition was related to performance on five tasks showing drug effects, confirming the postulated inverted U-shape relationship between drive and performance. 24 references. (Author abstract modified)

## 11 DRUG TRIALS IN MISCELLANEOUS DIAGNOSTIC GROUPS

**003591** Bacher, Norman M.; Lewis, Harvey A. Veterans Administration Mental Hygiene Outpatient Clinic, Federal Build-

ing, Baltimore, MD 21201 **Low-dose propranolol in tardive dyskinesia.** American Journal of Psychiatry. 137(4):495-497, 1980.

The effectiveness of treating tardive dyskinesia with propranolol was examined with 10 outpatients. Low doses of propranolol were added to the existing drug regimen of chronic psychiatric male patients. Seven patients showed significant improvement in their dyskinetic movements, especially in the oral-facial-buccal-lingual areas, and two of these patients improved dramatically. Side-effects were minimal and easily controlled by adjusting dosage. In some tardive dyskinesia patients, low dose propranolol has a markedly inhibitory effect. 10 references.

**003592** Bastani, J. Roman. Veterans Administration Hospital, 600 South 70th Street, Lincoln, NE 68510 **Physostigmine treatment of tricyclic overdosage in psychosis.** Psychosomatics. 20(12):847-848, 1979.

Two cases are reported which illustrate the complexity of physostigmine treatment of tricyclic overdosage in psychosis and the care required to handle it. The beneficial effects of physostigmine in the treatment of tricyclic overdosage, and the manifestation of the underlying psychosis after physostigmine was administered are demonstrated. It is suggested that symptomatic patients may require cardiac monitoring for several days before discharge in view of the slow excretion of the tricyclics. Underlying psychosis may surface during this period, and must be treated concomitantly. When indicated, phenothiazines are helpful in conjunction with the physostigimine. It is noted that the possibility of the anticholinergic action of certain phenothiazines' complicating the clinical signs of tricyclic overdosage requires the continuing alertness of the treating physician. 10 references.

**003593** Bateman, D. N.; Dutta, D. K.; McClelland, H. A.; Rawlins, M. D. Dept. of Pharmacological Sciences, Wolfson Unit of Clinical Pharmacology, University, Newcastle upon Tyne NE1 7RU, England **Metoclopramide and haloperidol in tardive dyskinesia.** British Journal of Psychiatry. 135(December):505-508, 1979.

The effect of single intravenous doses of metoclopramide (10, 20, 40mg) and haloperidol (5, 10mg) were compared to placebo (saline) in a double-blind randomized study in eight patients with tardive dyskinesia (TD) secondary to neuroleptic therapy. TD rating scores were improved significantly 6 hours after dosing by 40mg metoclopramide, and 5 and 10mg haloperidol when compared to placebo. Single doses of DA receptor blocking agents improved TD. The dose of metoclopramide required to show a beneficial effect was high, and this therefore suggests that it is unlikely to be of therapeutic value as the incidence of adverse reactions would be greatly increased. By monitoring the effects of single doses of DA receptor blocking drugs in patients with TD, it is possible to compare the relative potencies of these drugs on dopaminergic systems in vivo in man. 18 references. (Author abstract)

**003594** Boleloucky, Z.; Plevova, J.; Kamenicka, V.; Nahunek, K. Farmakologicky ustav LFH UK, Srobarova 50, Prague 10, Czechoslovakia **Item analysis of the differences in comparative drug effects as yielded by the self-rating questionnaire SCL-90.** Activitas Nervosa Superior. 21(2):123-124, 1979.

An item analysis of two scales used in a comparative drug study (SCL-90 and the 211-POPS) was undertaken to investigate differences in drug effects measured with the physician rating scale (211-POPS) and patient self-report scale (SCL-90). According to the psychiatrist's ratings, medazepam was more clinically effective than oxazepam or placebo in the treatment of 21 neurotic patients; while, according to the patient self-report questionnaire, oxazepam produced a significant reduction of difficulties, which medazepam and placebo did not. Questionnaire items specifically influenced by various drugs are identified, and the use of both physician rating scales and self-report inventories in pharmacotherapy research is discussed. 4 references.

**003595** Brown, Gerald L.; Ebert, Michael H.; Mikkelsen, Edwin J.; Hunt, Robert D. National Institutes of Health, Clinical Center, 9000 Rockville Pike, Bethesda, MD 20205 **Behavior and motor activity response in hyperactive children and plasma amphetamine levels following a sustained release preparation.** Journal of The American Academy of Child Psychiatry. 19(2):225-239, 1980.

Pharmacokinetic differences between tablets and sustained release d-amphetamine following single-dose administration were studied with nine hyperactive children. Observation of behavioral response and motor activity through a double-blind design indicated that significant clinical response is not observed beyond 4 hours and that responses occur only during the absorption phase and are not correlated with specific plasma levels of d-amphetamine. 47 references. (Author abstract modified)

**003596** Caine, Eric D.; Polinsky, Ronald J.; Ebert, Michael H.; Rapoport, Judith L.; Mikkelsen, Edwin J. Dept. of Psychiatry, University of Rochester Medical Center, 300 Crittenden Blvd., Rochester, NY 14642 **Trial of chlorimipramine and desipramine for Gilles de la Tourette syndrome.** Annals of Neurology. 5(3):305-306, 1979.

The effectiveness of chlorimipramine and desipramine were determined in a double-blind study of six patients with Gilles de la Tourette syndrome. Four of these patients had previously shown improvement with haloperidol treatment, while two experienced akathisia on haloperidol. With maximum daily doses of 150mg, chlorimipramine and desipramine both failed to show therapeutic effects. Tic frequency was not significantly improved, and one patient showed a marked exacerbation of symptoms on chlorimipramine. All patients showed some side-effects with this drug, and three also showed side-effects on desipramine. 5 references.

**003597** Campioni, A.; Russo-Perez, G. Reparto Neurologico, Ospedali, Civili Riuniti, Venice, Italy **/Pathogenetic hypothesis and a new therapeutic approach to delirium tremens./** Ipotesi patogenetiche e nuovo approccio terapeutico del delirium tremens. Rivista Sperimentale di Freniatria. 103(5);1587-1597, 1979.

The use of L-tryptophan in the therapy of delirium tremens (DT) was studied. The experimental sample of 20 subjects affected with DT were administered 2mg of L-tryptophan every 3 hours. The control group consisted of 20 subjects with analogous characteristics, who had recovered from DT the previous year. Results indicate that a significant decrease in length of DT episodes was found in the majority of the subjects. L-tryptophan did not demonstrate any toxicity or side-effects. It is concluded that these results might confirm the hypothesis that an alteration in dreaming patterns might be the cause of hallucinations in DT. 17 references. (Journal abstract modified)

**003598** Casey, Daniel E. Dept. of Psychiatry, Veterans Administration Medical Center, Portland, OR 97201 **Pharmacology of blepharospasm-oromandibular dystonia syndrome.** Neurology. 30(7, part 1):690-695, 1980.

The effects of dopaminergic and cholinergic drugs were evaluated in patients with blepharospasm and oromandibular dystonia (Meige Syndrome). The dopaminergic antagonist perphenazine and the cholinergic agonist deanol improved symptoms, whereas dopaminergic agonist (carbodopa/levodopa) and cholinergic antagonist (benzotropine) drugs had detrimental effects. Symptoms worsened during carbidopa/levodopa treatment but

temporarily resolved in one patient and improved in another than the drug was discontinued. Results suggest that Meige Syndrome is pharmacologically as well as clinically related to the hyperkinetic dyskinesias and that the symptoms involve an idiopathic form of receptor hypersensitivity. 31 references. (Author abstract modified)

**003599** Ciprian, Jorge. Centro de Investigaciones Diagnostico y Tratamiento en Neurociencias, Rodriguez Pena 1627, 1 piso, Capital Federal 1021, Argentina **Three cases of Gilles de la Tourette's syndrome. Treatment with chlorimipramine: a preliminary report.** Journal of Orthomolecular Psychiatry. 9(2):116-120, 1980.

Case reports are presented from successful treatment of Gilles de la Tourette Syndrome with chlorimipramine. The premature phobic and consequent later obsessive-compulsive development are identified as an important aspect of the disorder. The therapeutic value of chlorimipramine lies in its role as a serotonin uptake blocker. 27 references. (Author abstract modified)

**003600** Clare, Anthony W. no address **The treatment of premenstrual symptoms.** British Journal of Psychiatry. 135(December):576-579, 1979.

Research into the treatment of premenstrual symptoms is reviewed. A number of studies have reported favorable results with progesterone in the treatment of premenstrual depression and tension symptoms. However, a carefully controlled double-blind trail in 14 cases of premenstrual depression did not find it superior to spironolactone or placebo. Another study found significant improvement in weight gain and feeling bloated with dydrogesterone, but little improvement in psychological symptoms such as depression, irritability, and tension. Mixed results have been reported in the use of bromocriptine. Another recent study found reduction in weight gain and psychological symptoms using aldosterone and spironolactone. Another study reported significant improvement of premenstrual mood disturbance with bromocriptine, but two additional controlled studies failed to sustain this finding. Pyridoxine has also been reported successful in treatment, as has psychotherapy. Research into attitudinal factors and the role of stress in premenstrual tension syndrome may prove valuable. 49 references.

**003601** Clark, W. Crawford; Goetz, Raymond R.; McCarthy, Richard H.; Bemporad, Brenda; Zeidenberg, Phillip. no address. **Effects of marihuana on pain and verbal memory: a sensory decision theory analysis.** In: Nahas, G., Marihuana: biological effects. Oxford, Pergamon, 1979. 777 p. (p. 665-680).

Following theoretical descriptions of sensory decision, pain studies, and memory studies, the effects of marihuana on pain and verbal memory were studied in two experiments. Subjects were marihuana users who used no other drugs. For pain procedures, 20 thermal stimuli were presented at varied intensities in a random manner. For the memory procedures, subjects viewed 200 three consonant trigrams presented at the rate of one every 4 seconds. Results suggest that: 1) marihuana lacks any hypalgesic activity, and probably enhances the perception of pain; and 2) extremely heavy smokers showed a definite memory storage deficit, and perhaps an acquisition loss, in addition to a retrieval deficiency. 31 references.

**003602** Couch, James R.; Hassanein, Ruth S. Division of Neurology, Southern Illinois University School of Medicine, Box 3926, Springfield, IL 62704 **Amitriptyline in migraine prophylaxis.** Archives of Neurology. 36(11):695-699, 1979.

In a controlled trial of amitriptyline hydrochloride in migraine prophylaxis, 100 patients received placebo for a 4 week baseline period and then were randomized in double-blind fashion to therapy with amitriptyline (47 Ss) or placebo (53 Ss) for another 4 to 8 weeks. Ss received up to four 25mg tablets of amitriptyline hydrochloride or identical placebo per day. Comparing the first and second 4 week periods for each patient, the conditions of 55.3% of amitriptyline Ss as opposed to 34% of placebo Ss were greater than 50% improved and the difference between amitriptyline and placebo response rates was significant. Nondepressed Ss with severe migraine and depressed Ss with less severe migraine had little headache relief. It is concluded that amitriptyline is an effective antimigraine agent and the antimigraine effect seems relatively independent of antidepressant activity. 37 references. (Author abstract)

**003603** Crook, Thomas. Psychopharmacology Research Branch, Division of Extramural Research Program, NIMH, 5600 Fishers Lane, Rockville, MD 20857 **Central-nervous-system stimulants: appraisal of use in geropsychiatric patients.** Journal of the American Geriatrics Society. 27(10):476-477, 1979.

The CNS stimulants of methylphenidate and pentylenetetrazol were appraised to determine their efficacy in the treatment of aged persons with senility symptoms. A review of clinical studies conducted with these compounds indicates that firm evidence of efficacy is lacking. Because of the risks associated with high doses of such stimulants in the aged, it was concluded that the extensive use of these compounds in geriatric psychiatry should be discouraged. 5 references. (Author abstract)

**003604** Daokuan, Liu; Yuping, Jiang. Dept. of Neurology, Shanghai First Medical College, Shanghai, China **Long-term effects of home-made levodopa in 43 cases of paralysis agitans.** Chinese Medical Journal. 92(11):807-810, 1979.

The therapeutic efficacy of homemade levodopa (L-dopa) was investigated in 43 cases of idiopathic Parkinson's disease. L-dopa was effective in 30 of these cases (69.8%), giving excellent results in eight, good results in 15 and fair results in seven. In 12 of the 30, medication effect tapered during 2 year long-term therapy, and long-term therapy did not arrest progression of the disease. Long-term side-effects included dyskinesia, which was tolerable in most patients, on/off alternating dyskinesia, akinesia, kinesia paradoxica, and mental symptoms. L-dopa was required in large doses; most of the ingested dose enters extracerebral tissue where DA and some of its metabolites may induce many side-effects such as gastrointestinal and cardiovascular reactions. Compounds of dopa decarboxylase inhibitor and L-dopa available in two preparations gave better results than L-dopa alone but did not reduce extracerebral side-effects. DA receptor agonists also gave encouraging results; and further research is planned. 10 references. (Author abstract modified)

**003605** Dawling, S.; Crome, P.; Braithwaite, R. Poisons Unit, Guy's Hospital, London, SE1 9RT, England **Pharmacokinetics of single oral doses of nortriptyline in depressed elderly hospital patients and young healthy volunteers.** Clinical Pharmacokinetics. 5(4):394-401, 1980.

A single oral dose of 75mg nortriptyline was given to a group of 20 depressed elderly patients in the hospital. Subsequent plasma nortriptyline concentrations were used to calculate the half/life and clearance of the drug. These measurements were compared with those made previously in 17 healthy young volunteer subjects. Plasma nortriptyline half life was longer and clearance slower in the elderly group than in the volunteers. There was no correlation of age with either of these parameters within the two groups, and no differences in nortriptyline pharmacokinetics could be detected between the male and female volunteer subjects. The reasons for these findings and their clinical consequences are discussed. 27 references. (Author abstract)

**003606** Doenecke, Arthur L.; Heuermann, Robert C. 236 North Duke St., Lancaster, PA 17602 **Treatment of haloperidol abuse with diphenhydramine.** American Journal of Psychiatry. 137(4):487-488, 1980.

The effects of diphenhydramine on haloperidol toxicity were examined with five adolescents. The drug's extrapyramidal side-effects such as dystonia, dyskinesia, and akathisia were successfully treated with diphenhydramine following overdoses of haloperidol. The signs and symptoms of haloperidol toxicity observed were similar to those previously reported. It is suggested that diphenhydramine is the drug of choice in treating haloperidol toxicity. 4 references.

**003607** Famuyiwa, O. O.; Eccleston, D.; Donaldson, A. A.; Garside, R. F. Eccleston: Dept. of Psychiatry, Royal Victoria Infirmary, Newcastle upon Tyne, England **Tardive dyskinesia and dementia.** British Journal of Psychiatry. 135(December):500-504, 1979.

The incidence of dementia was examined in 17 schizophrenic patients with tardive dyskinesia (TD) and 33 schizophrenics without TD using psychological tests of intellectual function and EMI scans. The group as a whole were found to be demented, and 31 out of 45 had abnormalities on the scan. On a learning test, TD subjects performed significantly worse; and using a measured parameter of the scan (the ventricular index), the TD group had more abnormality. It is suggested that the higher incidence of pathology in the TD group may be related to chronic neuroleptic toxicity. 16 references. (Author abstract modified)

**003608** Finzen, C.; Kruse, G. Kruse: Am Kanonenwall 1, D-3000 Hannover 1, Germany **/Combination therapy of delirium tremens with haloperidol and clomethiazol./** Kombinationstherapie des Alkoholdelirs mit haloperidol und clomethiazol. Psychiatrische Praxis. 7(1):50-56, 1980.

Based on theoretical considerations regarding delirium tremens as a form of psychosis, the additional application of a neuroleptic with an antipsychotic action is suggested as a specific treatment exercising a direct influence both on the psychotic and the neurovegetative signs of alcoholic delirum. Experiences, extending over a 2 year period, with intravenously administered haloperidol and oral clomethiazol pointed to a decrease in the incidence rate of delirium, a milder course of delirium itself, and a corresponding decrease in associated complications. Findings should stimulate further systematic and statistically supported investigations in this field. 25 references. (Author abstract modified)

**003609** Holsey, Chandra Varnetta. State University of New York at Buffalo **Attentional performance in hyperkinetic children: an investigation of the relationship between methylphenidate, stimulus exposure duration and inter-trial interval. (Ph.D. dissertation).** Dissertation Abstracts International. 40(1):452-B, 1979. Ann Arbor, Univ. Microfilms No. 7913892, 113p., 1979.

The relationship between stimulus exposure duration and intertrial interval on the attentional performance of hyperkinetic children was investigated using the Continuous Performance Test (CPT) and the maximum effect of this manipulation in the presence and absence of methylphenidate (Ritalin) was studied. Eight outpatient children, between the ages of 6 and 12, served as subjects in this 10 week, double-blind, crossover study. Hyperkinetic children achieved greater accuracy on the CPT as both exposure duration and intertrial intervals increased. No significant difference was noted between the two drug treatment conditions; however, this is attributed in part to parents' refusal to let children participate in the placebo condition or withdrawing children from the study due to intolerable although characteristic behavior. (Journal abstract modified)

**003610** Houillon, P.; Kitenge, A.; Jouannigot, R.; Lullien, L.; Cadic, F. no address **/Observations concerning some therapeutic effects of piracetam (part 1)./** Remarques sur quelques effets therapeutiques du piracetam (1re partie). Annales Medico-Psychologiques. 137(6-7):605-610, 1979.

Therapeutic effects of piracetam (2-oxo-1 pyrrolidine acetamide) were used to treat oligophrenias of 35 children and two cases of 70-year-old patients suffering from pre-senile abiotrophic dementia and related syndromes. The drug is also used for treatment of epilepsy and various cerebral attacks (traumatic, vascular, and toxic). It was found that in several cases most of the following four pharmacological properties of the drug were confirmed: 1) facilitation of information transfer from one cerebral lobe to the other, 2) faciliation of learning and memorization, 3) reinforcement of cortical control of subcortical neuronic structures, and 4) protection of the brain against hypoxia. A discussion follows the text of the article. 13 references.

**003611** Jorgensen, Ole Sylvester; Lober, Marianne; Christiansen, Johannes; Gram, Lars F. Gram: Dept. of Clinical Pharmacology, Odense University, J. B. Winslows Vej 19, DK-5000 Odense C, Denmark **Plasma concentration and clinical effect in imipramine treatment of childhood enuresis.** Clinical Pharmacokinetics. 5(4):386-393, 1980.

The relationship between steady-state plasma concentration and clinical effect of imipramine in the treatment of nocturnal enuresis was studied in 22 hospitalized children. After 1 week on placebo the children were given imipramine in a fixed dose of about 1mg/kg for 3 weeks. The enuresis frequency decreased significantly from the placebo to the first week on imipramine, but then no further improvement was observed. There was significant correlation between steady-state plasma concentration of desipramine or imipramine plus desipramine and the reduction in enuresis frequency during imipramine treatment. The optimum effect was obtained when steady-state levels of imipramine plus desipramine were above 60mcg. Dose corrected and weight corrected, steady-state plasma concentrations of imipramine and desipramine were not significantly different from those previously observed in younger adults. In one child, a transient rise in imipramine and desipramine concentration was seen during a period with fever and bacterial infection. 8 references. (Author abstract)

**003612** Juchau, M. R.; Chao, S. T.; Omiecinski, C. J. Dept. of Pharmacology, School of Medicine, SJ-30, University of Washington, Seattle, WA 98195 **Drug metabolism by the human fetus.** Clinical Pharmacokinetics. 5(4):320-339, 1980.

Literature that pertains to drug biotransformation in human fetal tissues is reviewed. A large majority of the studies have dealt with the cytochrome P-450 dependent microsomal monooxygenase systems. Some of the more important data that have emerged include observations that important bioactivation reactions can be demonstrated in human fetal tissues obtained during the period of late embryogensis. Most data indicate that the biotransformation of drugs in the human embryo would not affect maternal plasma concentrations significantly. The demonstrated capacity of human prenatal tissues and cells to generate reactive intermediary metabolites has attracted the greatest attention. This capacity may be associated with important adverse reactions to drugs and other environmental chemicals. Such responses include transplacental mutagenesis, carcinogenesis, and dysmorphogenesis. The data suggest that humans and subhuman primates may be more vulnerable than the smaller common experimental animals to the toxic effects of foreign organic chemi-

cals during prenatal life. It is concluded that these factors should be weighed whenever exposure of pregnant women to such agents is contemplated. 125 references. (Author abstract modified)

**003613** Krabbe, Annette Aebelholt; Olesen, Jes. Dept. of Neuromedicine, Rigshospitalet, Copenhagen, Denmark **Headache provocation by continuous intravenous infusion of histamine, clinical results and receptor mechanisms.** Pain. 8(2):253-259, 1980.

Histamine was infused intravenously in 13 normal Ss, 10 patients with chronic muscle contraction headache, and 25 patients with common migraine. Histamine did not induce pulsating headaches in the normal Ss, but was associated with headaches in all but one patient in each of the headache groups. Headaches disappeared when the histamine infusions were terminated or when the H1 histamine blocking agent mepyramine was injected. The H2 blocker cimetidine was less effective. 23 references. (Author abstract modified)

**003614** Levy, Florence. University of New South Wales (Australia) **Developmental hyperkinesis. (M.D. dissertation).** Dissertation Abstracts International. 40(11):5205-B, 1980. (Not available from Univ. Microfilms), 1979.

The development and evaluation of measures of hypactivity, attention deficits, and impulsivity (the three central features of the hyperkinetic syndrome) are described. Three studies which established age norms and gender relationships of measures of attention and inhibition, investigated the relationship between measures of motility and attention and inhibition, and assessed the performance of a behavioral disordered group of children on these measures, are described. Also, a hyperkinesis factor obtained from these data was validated on three groups of clinic children diagnosed as manifesting moderate to severe hyperkinesis. The effects of methylphenidate on hyperkinesis factor scores were also assessed. Results suggest that a factor derived from age normalized data using measures of sustained attention, motor inhibition, and motility is a useful instrument for diagnosis and measurement of treatment effects in hyperkinetic children. (Journal abstract modified)

**003615** Lieberman, A.; Neophytides, A.; Kupersmith, M.; Casson, I.; Durso, R.; Foo, S. H.; Khayali, M.; Tartaro, T.; Goldstein, M. Dept. of Neurology, New York University Medical Center, 530 First Avenue, Suite 5A, New York, NY 10016 **Treatment of Parkinson's disease with dopamine agonists: a review.** American Journal of the Medical Sciences. 278(1):65-76, 1979.

Bromocriptine and lergotrile were administered to 81 patients with Parkinson's disease and increasing disability despite optimal treatment with levodopa (secondary levodopa failures). Sixty-six patients were treated with bromocriptine and 53 patients were treated with lergotrile. Both groups had significantly decreased rigidity, tremor, bradykinesia, and gait disturbance upon addition of bromocriptine or lergotrile to levodopa. Twenty-five patients improved at least one stage on bromocriptine, and 21 improved at least one stage on lergotrile. The mean dose of bromocriptine was 47mg, and the mean dose of lergotrile was 49mg, permitting a 10% reduction in levodopa. Bromocriptine was discontinued in 29 of 66 patients because of adverse effects, including mental changes (14 patients) and involuntary movements (9 patients). Lergotrile was discontinued in 33 of 53 patients because of adverse effects including hepatotoxicity (11 patients) and mental changes (12 patients). The results of treatment with bromocriptine or lergotrile were comparable, with patients either responding or not. Bromocriptine will shortly be available for use, but lergotrile, because of the hepatotoxicity, will not. 80 references. (Author abstract)

**003616** Luborsky, L.; Ancona, L.; Masoni, A.; Scolari, G.; Longoni, A. Hospital of the University of Pennsylvania, 207 Piersol Building, G1, Philadelphia, PA 19104 **Behavioral versus pharmacological treatments for essential hypertension: a pilot study.** International Journal of Psychiatry in Medicine. 10(1):33-40, 1980.

The comparative efficacy of a behavioral approach (autogenic training) and pharmacological therapy for the treatment of essential hypertension was investigated. Fifteen essential hypertension Ss were assigned to one of three treatment conditions: 1) autogenic training; 2) pharmacological treatment (usually a diuretic such as thiazide); or 3) both behavioral and pharmacological treatment. The group given antihypertensive medication was significantly more improved (as determined by blood pressure decrease) buy the fourth quarter of the treatment as compared with the relaxation treatment or with the combination. This advantage for routine amounts of antihypertensive medications vs. behavioral treatments is consistent with the only other data from similar comparison that is available. 10 references. (Author abstract modified)

**003617** Mackay, Angus V. P.; Sheppard, Graham P. MRC Neurochemical Pharmacology Unit, Cambridge University Medical School, New Addenbrooke's Hospital, Cambridge CB2 2QD, England **Pharmacotherapeutic trials in tardive dyskinesia.** British Journal of Psychiatry. 135(December):489-499, 1979.

Following consideration of some of the clinical factors contributing to the currently unsatisfactory state of therapy for tardive dyskinesia, pharmacological research is reviewed. Problems such as lack of clear syndrome delineation and phenomenological description, lack of standardization of rating scales, and the lack of attention to trial design have all probably contributed to a rather confusing picture. Pharmacotherapeutic trials involving DA receptor antagonists, DA depleting drugs, DA mimetic drugs, cholinergic drugs, GABAacidic drugs, and others such as lithium and papaverine are summarized. Controlled trials suggest that several pharmacological agents may have therapeutic value, but that clinical prediction of an individual's response is impossible. The strategy of acute drug challenge has emerged as perhaps the most promising approach to the definition of pharmacological subtypes, and therefore, the choice of optimal treatment. 56 references. (Author abstract modified)

**003618** Mairlot, F. Regentiestraat 18, B-2700 Sint-Niklaas, Belgium **/Analysis of results obtained with depamide in children with psychomotor instability (hyperkinesis)./** Analyse des resultats obtenus avec le depamide chez des enfants atteints d'instabilite psychomotrice (hyperkinesie). Acta Psychiatrica Belgica. 79(2):210-224, 1979.

Results from 10 years of observations of children with psychomotor instability (hyperkinesis) generally due to minimal brain dysfunction, are presented. A clinical summary emphasizes the instability and difficult coordination of all aspects of the personality. A pathogenic hypothesis concerns one of the stimulation functions which may be abnormal, as the control and regulation of personality, partly located at the subcortical level and creating secondary symptoms and reactional ones. The results of therapy are interpreted according to a clinical research protocol which proposes a global appreciation, an appreciation of the duration of therapeutic effect through the study of variation of specific criteria, and a general appreciation correlating both aspects. Through this methodology and the mean duration of treatment of two years, the results were significant in 55% of the cases. Compared to other drugs, depamide seemed more valid and was without secondary clinical and psychological effects. 5 references. (Journal abstract modified)

**003619** Michael, Robin Lynn. University of Rochester **The effect of methylphenidate on hyperactive children's evoked potentials. (Ph.D. dissertation).** Dissertation Abstracts International. 41(1):360-B, 1980. Ann Arbor, Univ. Microfilms No. 8014335, 136p., 1980.

The effects of methylphenidate on hyperactive children's performance and evoked potentials during sustained attention as well as their deviations from normality were investigated. Seventeen White hyperactive boys and four hyperactive girls between the ages of 6.2 and 12.7 years were tested in two sessions during which they received an acute dose of methylphenidate or placebo in counterbalanced order. Twenty-one normal children matched on age, sex, and race were tested in two sessions without medication. For both samples, evoked potentials were obtained during two continuous performance test procedures which differed in range of levels of stimulus relevance. In comparison to normal children, hyperactive children tested under placebo made more errors of omission and commission on both tasks. In addition, it was found that methylphenidate generally increased the amplitude of hyperactive Ss' late positive components and improved their accuracy on the test. During the passive task, differences in late positive component amplitude between normals and hyperactives Ss did not emerge and methylphenidate did not have any consistent effect on hyperactive Ss' late positive components. (Journal abstract modified)

**003620** Oscar-Berman, Marlene; Gade, Anders; Feldman, Robert G.; Saavedra, M. A. Aphasia Research Center, Boston Veterans Administration Hospital, 150 S. Huntington Ave., Boston, MA 02130 **Effects of dimepramine fumarate on physiological and cognitive behaviors of Parkinson patients.** Journal of Clinical Pharmacology. 19(10):626-634, 1979.

Electrodermal responsiveness to unpredictable loud sounds was tested in nine patients with Parkinson's disease before and after treatment with 50 to 225mg/day of dimepramine fumarate for 3 weeks. Results showed that the drug tends to decrease autonomic arousal responses, as measured by resting conductance levels, number of fluctuations in skin conductance per minute, orienting response, and habituation rate. These decreases in electrodermal measures of arousal were generally accompanied by lowered performance scores on several tests of memory and temporal discrimination ability. 13 references.

**003621** Parkes, J. D.; Schachter, M. Dept. of Neurology, King's College Hospital, London SE5, England **Mazindol in the treatment of narcolepsy.** Acta Neurologica Scandinavica. 60(4):250-254, 1979.

Thirty-four Ss with narcoleptic syndrome were treated with mazindol, a tricyclic compound with little or no effect on mood, for 1 year. caused a sustained improvement in narcolepsy, but had no effect on cataplexy or sleep paralysis. The response to mazindol was excellent in six Ss, good in 14 Ss, moderate in 12 Ss, and poor in two. No cardiovascular effects, hematological toxicity, tolerance or dependence occurred. Mazindol 6mg had the same effect on narcolepsy as d-amphetamine 50mg, but caused less side-effects. 9 references. (Author abstract modified)

**003622** Pelham, William E.; Schnedler, Robert W.; Bologna, Nancy C.; Contreras, J. Anthony. Dept. of Psychology, Florida State University, Tallahassee, FL 32306 **Behavioral and stimulant treatment of hyperactive children: within-subject design.** Journal of Applied Behavior Analysis. 13(2):221-236, 1980.

Behavioral and stimulant treatment were investigated in eight hyperactive children treated with a behavioral intervention focusing on teacher and parent training. The children also received before and during therapy methylphenidate, either .25/mg/kg or .75mg/kg. Classroom observations suggested that effectiveness was between that of the two dosages of medication before therapy. Both dosages resulted in higher levels of on task behavior when administered after 13 weeks of behavioral intervention. As a group, only when they received the high dose of methylphenidate after 13 weeks did children reach the level of appropriate behavior. The results suggest that the combination of psychostimulant medication and behavior therapy may be more effective in the short-term than either treatment alone for hyperactive children in school settings. In addition, parent ratings and clinic observation of parent-child interactions suggested that children had improved in the home setting, highlighting the importance of behavioral parent training in the treatment of hyperactivity. 43 references. (Author abstract modified)

**003623** Perris, Carlo; Dimitrijevic, Predrag; Jacobsson, Lars; Paulsson, Paul; Rapp, Walter; Froberg, Hans. Dept. of Psychiatry, Umea University, Umea S-901 85, Sweden **Tardive dyskinesia in psychiatric patients treated with neuroleptics.** British Journal of Psychiatry. 135(December):509-514, 1979.

The point of prevalence of tardive dyskinesia (TD) as assessed by the Simpson rating scale was determined for 14 psychiatric wards with 347 patients (213 male and 134 female). TD was found to occur in 17.3% of the patients, with prevalence significantly higher for females. Frequency of TD was found to increase with age. A comparison of a random group of TD and non-TD patients revealed no differences between groups for total amount of high or low dosage neuroleptics or anticholinergic drugs. However, significantly more TD patients had received anticholinergic drugs. There was no significant relationship between TD severity and age, duration of treatment, or total amount of high or low dose neuroleptics. A significant relationship was found between TD severity and amount of anticholinergic drugs. Significantly more TD patients than controls had a past history which might suggest possible brain damage prior to neuroleptic medication. 29 references. (Author abstract modified)

**003624** Perry, Thomas L.; Wright, James M.; Hansen, Shirley; Allan, Barbara M.; Baird, Patricia A.; MacLeod, Patrick M. Dept. of Pharmacology, University of British Columbia, Vancouver, BC, Canada V6T 1W5 **Failure of aminooxyacetic acid therapy in Huntington disease.** Neurology. 30(7, part 1):772-775, 1980.

Seven patients with Huntington disease were treated with aminooxyacetic acid (AOAA), an inhibitor of GABA aminotransferase (GABA-T) activity. Toxic symptoms (drowsiness, ataxia, seizures, and psychotic behavior) were seen in all seven patients when AOAA dosage was increased above 2mg/kg/day. No clinical improvement was observed in the five patients who took AOAA for 4 months. AOAA was not as effective as large doses of isoniazid in inhibiting hepatic GABA-T enzyme activity. 14 references. (Author abstract modified)

**003625** Primrose, D. A. Royal Scottish National Hospital, Larbert, Stirlingshire, FK5 4EJ, Scotland **Treatment of self-injurious behaviour with a GABA (gamma-aminobutyric acid) analogue.** Journal of Mental Deficiency Research. 23(Part3):163-173, 1979.

Self-injurious and other undesirable behavior is described in 28 mental defectives in a hospital, and the effect of treatment with a GABA analogue is given. Twenty-two of the patients who were severely subnormal and whose behavior improved after commencing bacoflen were then followed up for 20 weeks in a double-blind cross-over trial. There was significant improvement in the behavior of many of the patients. In some patients the improvement seemed to be dependent on continuing the baclofen, while in others it has been maintained after stopping the drug, thus indicating that behavior modification took

place. It is reported that it has been possible to discontinue, or reduce, other medication in some of the patients. The results of the treatment, including side effects, are discussed. 9 references.

**003626** Raskind, Murray; Alvarez, Carrol; Herlin, Susan. GRECC/1828, Seattle V.A. Medical Center, 4435 Beacon Avenue South, Seattle, WA 98108 **Fluphenazine enanthate in the outpatient treatment of late paraphrenia.** Journal of the American Geriatrics Society. 27(10):459-463, 1979.

Fluphenazine enanthate parenterally was compared to an antipsychotic drug (haloperidol) given orally for the intervention" treatment of elderly outpatients with late paraphrenia. In the fluphenazine group, 11 of 13 patients improved, compared to only 3 of 13 in the oral drug group (p is less than 0.01). The superiority of fluphenazine probably was attributable to improved compliance with the prescribed regimen by patients receiving parenteral depot medication. Despite the advanced age of the subjects, significant adverse drug effects were uncommon. It is emphasized that depot fluphenazine enanthate is not recommended as the drug of choice for the inpatient treatment of late paraphrenia or in the treatment of outpatients for whom compliance with an oral antipsychotic drug regimen can be assured by careful supervision. However, low dosage intramuscular fluphenazine enanthate can play an important role in the seriously ill and treatment resistant patient with late paraphrenia, whose continued ability to live independently in the community depends upon rapid remission of psychotic symptoms. 15 references. (Author abstract)

**003627** Ritterman, Michele Klevens. Temple University **Outcome study for family therapy, Ritalin and placebo treatments of hyperactivity: an open systems approach. (Ph.D. dissertation).** Dissertation Abstracts International. 39(12):6138-B, 1979. Ann Arbor, Univ. Microfilms No. 7910077, 253p., 1978.

In a controlled double-blind study of the role of the family in the treatment of the hyperactive child, 40 (6 to 11 year old) boys were randomly assigned to a family therapy (FT), Ritalin (R), FT/R, or FT/placebo (FT/P) group. Results suggested that treatment did not differ significantly on any single index and that improvement was significant for the majority of indices examined. It is suggested that cost effectiveness and potential side-effects of R or FT must be considered in determining treatment of choice. A trend toward a main effect of family type was also found. Additionally, findings rule out a pattern of significant interactions between high/low severity behavioral, self-concept, and attentional subgroups and treatment conditions for any one of the eight indices of hyperactivity. Additional findings relating to placebo effects, duration of treatment and family/therapist rapport, and followup outcomes at 3 to 5 months are discussed. An open systems family structural approach is used in interpretating results. (Journal abstract modified)

**003628** Roccatagliata, G.; Maffini, M.; Cocito, L.; Gandolfo, C.; Seneghini, A.; Romei, T.; Albano, C. Clinica Neurologica, Universita Genova, Genoa, Italy **/Alcoholism and apomorphine: a catamnestic study./** Alcoolismo e apomorfina: studio catamnestico. Minerva Psichiatrica. 20(4):245-247, 1979.

A catamnestic investigation of 30 chronic alcoholics who underwent a clinical deconditioning trial therapy with apomorphine is reported. The treatment included a brief course of psychotherapy and proved effective. At the end of the 1 to 7 year observation period, more than 70% of the patients remained free of their previous addiction to alcohol. 8 references. (Journal abstract modified)

**003629** Roccatagliata, Giuseppe; Albano, Claudio; Cocito, Leonardo; Maffini, Maura. Clinica Neurologica, Via A. de Toni 5, I-16132 Genoa, Italy **Interactions between central monoaminergic systems: dopamine-serotonin.** Journal of Neurology, Neurosurgery, and Psychiatry. 42(12):1159-1162, 1979.

Concentrations of dopamine and serotonin metabolites (homovanillic acid; HVA and 5-hydroxyindoleacetic acid; 5-HIAA) in the cerebrospinal fluid were evaluated before and after pharmacological treatment in 19 patients with different neuropsychiatric diseases. In every case, a reciprocal modification of the two metabolites occurred after treatment. Results support the hypothesis of a functional balance between the monoaminergic systems in the CNS. Diagnostic groups and drugs administered included: Huntington's chorea, endogenous depression, acute schizophrenic reaction, undifferentiated type, chronic schizophrenic reaction, paranoid type, tardive dyskinesia, chlorimipramine, haloperidol, trazodone, imipramine, amitriptyline, fluphenazine, and baclofen. 23 references. (Author abstract modified)

**003630** Rylance, George W.; Moreland, Terence A. Dept. of Child Health, Ninewells Hospital and Medical School, Dundee DD1 9SY, Angus, Scotland **Drug level monitoring in paediatric practice.** Archives of Disease in Childhood. 55(2):89-98, 1980.

Problems involved with monitoring drug levels in the field of pediatrics are discussed. In determining the therapeutic range of a particular drug a variety of factors must be considered, including dose regimen, active metabolites, combination therapy, patient compliance and assay reliability. Therapeutic drug monitoring levels of specific anticonvulsants including pheytoin, phenobarbitone, primidone, carbamazepine, sodium valproate, diazepam, ethosuximide, digoxin, theophylline, salicylate and for the antibacterial drugs gentamicin, tobramycin, and chloramphenicol are discussed. Drug monitoring using other body fluids such as cerebrospinal fluid and saliva is described. 151 references.

**003631** Sachdev, Harmeet S.; Brodsky, Lewis. Brodsky: Mt. Carmel Professional Bldg., Suite 421, 6001 West Outer Drive, Detroit, MI 48235 **Lithium carbonate: a therapeutic agent for spasmodic torticollis.** Psychosomatics. 20(12):831, 834-836, 1979.

Current treatment approaches for spasmodic torticollis are reviewed with special emphasis on the pharmacologic approach. No therapy has yet provided consistently good results. Case histories of two patients are presented, both refractory to other treatment approaches, who responded to lithium carbonate. Lithium may be most specifically indicated for patients with a coexisting affective disorder. 19 references. (Author abstract)

**003632** Schachter, M.; Parkes, J. D. Parkes: Institute of Psychiatry, King's College Hospital, London SE5, England **Fluvoxamine and clomipramine in the treatment of cataplexy.** Journal of Neurology, Neurosurgery, and Psychiatry. 43(2):171-174, 1980.

Fluvoxamine (25 to 200mg daily) and clomipramine (25 to 200mg daily) were given for separate 3 week periods to 18 Ss with narcolepsy and cataplexy. Both drugs improved cataplexy but not narcolepsy. Fluvoxamine was less active than clomipramine and delayed ejaculation in two men from clomipramine. Fluvoxamine is a more potent inhibitor of 5-hydroxytryptamine (5-HT) reuptake in some systems, but not in others. It is therefore uncertain whether the greater anticataplectic effect of clomipramine is due to a greater inhibition of 5-HT reuptake or to other mechanisms. 21 references. (Author abstract modified)

**003633** Schmitt, H. Dept. de Pharmacologie, Faculte de Medecine Broussais, 15, rue de l'Ecole-de-Medecine, F-75270 Paris Cedex 6, France **/Mechanism of action of anorexigenic drugs./** Mecanisme d'action des anorexigenes. Therapie. 34(2):155-179, 1979.

The sites and mechanisms of action involving neurotransmitters in actions of anorexigenic drugs are reviewed. The anorexigenic drugs are often prescribed for patients who need to lose weight. Central dopaminergic and 5-hydroxytryptaminergic mechanisms are able to reduce food intake although noradrenergic mechanisms increase food consumption. Pharmacological properties of classical amphetamine like drugs are compared to those of fenfluramine. The amphetamine types can be ascribed to a dopamine release, but the fenfluramine properties are probably due to 5-hydroxytryptaminergic mechanisms. The anorexigenic actions must be ascribed to the 5-hydroxytryptaminergic mechanisms also. 123 references. (Journal abstract modified)

**003634** Schneider, E.; Fischer, P.-A.; Jacobi, P.; Becker, H.; Beyer, M. Abteilung fur Neurologie, Klinikum der Universitat, Schleusenweg 2-16, D-6000 Frankfurt am Main, Germany **Cerebral atrophy and long-term response to levodopa in Parkinson's disease.** Journal of Neurology. 222(1):37-43, 1979.

In 92 parkinsonian patients (42 men, 50 women) from 37 to 79 years old, the impact of cerebral atrophy as assessed by computed tomography (CT) on the course of the clinical symptomatology under levodopa during a period of 1 to 5 years was investigated. It was shown that patients suffering from medium to severe degrees of atrophy, independent of its special location, had a less favorable response than those with normal CT findings. The data do not allow a definite decision on whether cortical atrophy or ventricular enlargement is of major importance. The width of the third ventricle seemed to have no influence on the course of the clinical symptoms. After 3 years of levodopa treatment a dissociation between cerebral atrophy and therapeutic effectiveness was observed. 33 references. (Journal abstract)

**003635** Shouse, M. N.; Lubar, J. F. VA Medical Center, Sepulveda, CA **Operant conditioning of EEG rhythms and ritalin in the treatment of hyperkinesis.** Biofeedback and Self-Regulation. 4(4):299-312, 1979.

The application of sensorimotor rhythm (SMR) operant conditioning to hyperkinesis uncomplicated by a history of epilepsy was studied. EEG and behavioral indices were monitored in four hyperkinetic children under the following six conditions: no drug, drug only, drug and SMR training I, drug and SMR reversal training, drug and SMR training II, no drug and SMR training. Combining medication and SMR training resulted in substantial improvements that exceeded the effects of drugs alone and were sustained with SMR training after medication was withdrawn. Pretraining levels of SMR accurately reflected both the severity of original motor deficits and the susceptibility of hyperkinetic subjects to both treatments. Despite certain qualifications, it is suggested that SMR has prognostic and diagnostic value in the disorder when overactivity rather than distractibility is the predominant behavioral deficit. 21 references. (Author abstract modified)

**003636** Sironi, Vittorio A.; Cabrini, Gianpiero; Porro, Maria G.; Ravagnati, Luigi; Marossero, Franco. Via L. Briante, 98, I-21019 Somma Lombardo (VA), Italy **Antiepileptic drug distribution in cerebral cortex, Ammon's horn, and amygdala in man.** Journal of Neurosurgery. 52(5):686-692, 1980.

The concentrations of phenobarbital, phenytoin, and carbamazepine in plasma, cerebrospinal fluid, and brain in surgically treated epileptic patients were analyzed. The three drugs were uniformly distributed in the gray and white matter in different brain areas (except for a higher concentration of phenobarbital in the rhinencephalic structures in comparison with the corresponding temporal neocortex) and in normal and scar tissue. The findings suggest that in therapy resistant patients, anticonvulsant drugs are pharmacologically ineffective, despite the fact that the cerebral drug concentrations are at therapeutic levels or higher. 38 references. (Author abstract modified)

**003637** Stalpes, Bunny. Center for Human Services, 4340 East-West Highway, Bethesda, MD 20014 **Learning about the elderly -- closing the gaps.** American Pharmacy. NS20(5):19-23, 1980.

The need for pharmacists to understand the needs of the elderly and to advocate a rational approach to drug use is addressed. A special project, whose goal was to identify the pharmaceutically related needs of the elderly and to make recommendations for meeting these needs through pharmacy education programs at both the undergraduate and the continuing education level, is described. The project emphasized the need for effective communication between pharmacist and elderly client, since the former must often play a critical role as consultant, advocate, and teacher for elderly patients faced with the increasingly complex world of pharmacological treatment for physical and mental disorders. To achieve such effectiveness, the pharmacists must understand the pharmacokinetic changes in a drug's effects that occur with age, and specific attention must be paid to training pharmacy students in the biomedical and psychosocial needs of the elderly. 3 references.

**003638** Sundaresan, P. R.; Wardell, William M.; Weintraub, Michael; Lasagna, Louis. Weintraub: Dept. of Pharmacology, University of Rochester, 601 Elmwood Ave., Rochester, NY 14642 **Methodology for demonstrating sustained efficacy of hypnotics: a comparative study of triazolam and flurazepam.** Clinical Pharmacology and Therapeutics. 25(4):391-398, 1979.

Chronic insomniac patients were treated for seven consecutive nights with 0.6mg triazolam or 30mg flurazepam in a parallel, double-blind design. Both drugs showed sustained hypnotic efficacy with no appreciable hangover effects. No significant differences were observed between mean scores on the first two nights of the study and those on the last two nights, but first night results tended to be atypical. Methodological problems in the measurement of the sustained effects of hypnotics in repetitive dose trials are discussed. 9 references. (Author abstract modified)

**003639** Tamminga, Carol A.; Chase, Thomas N. Experimental Therapeutics Branch, NINCDS, NIH, 9000 Rockville Pike, Bethesda, MD 20205 **Bromocriptine and CF 25-397 in the treatment of tardive dyskinesia.** Archives of Neurology. 37(4):204-205, 1980.

The efficacy of two ergot derivatives, bromocriptine and CF 25-397, both possessing dopamine agonist properties, in the treatment of tardive dyskinesia was evaluated. The two drugs were administered at relatively low doses to eight neuroleptic free schizophrenic patients with tardive dyskinesia. Neither agent significantly improved dyskinetic symptoms; no symptoms worsened. Dopamine agonists likely vary in their selective activation of functionally distinct dopamine receptors. 25 references. (Author abstract modified)

**003640** Tolosa, Eduardo S.; Lai, Chi-wan. Box 468, University of Minnesota Hospitals, Minneapolis, MN **Meige disease: striatal dopaminergic preponderance.** Neurology. 29(8):1126-1130, 1979.

A dopamine agonist (apomorphine) and a cholinomimetic drug (physostigmine) were administered to five patients with blepharospasm and oromandibular dystonia (Meige disease). The effects of haloperidol and levodopa were also assessed. Apomorphine lessened and physostigmine aggravated the facial dyskinesias in all patients, while placebo injections had no consistent effect. Levodopa did not modify the symptoms, but haloperidol attenuated the facial dystonia. Dysfunction of the basal ganglia, characterized by a state of striatal dopamine preponderance,



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probably underlies the dystonic spasms in Meige disease. The prominent cholinergic enhancement of facial dyskinesias may distinguish this disorder pharmacologically from tardive dyskinesia, a differentiation which has practical therapeutic implications. 38 references. (Author abstract)

**003641** Tyrer, Peter; Gardner, Martin; Lambourn, John; Whitford, Mervyn. University Dept. of Psychiatry, Royal South Hants Hospital, Graham Road, Southhampton S09 4PE, England **Clinical and pharmacokinetic factors affecting response to phenelzine.** British Journal of Psychiatry. 136(April):359-365, 1980.

The relative importance of dosage, diagnosis, acetylator status, sex, and patient status in determining clinical response to the monoamine oxidase inhibitor phenelzine was studied. Thirty patients with depressive neurosis, 15 with anxiety neurosis and 14 with phobic anxiety states were treated with 15mg daily after which the dosage was increased to 30mg daily between the third and seventh day. Then, using double-blind procedure, one group took 45mg daily and the other took 90mg daily. The results suggest that dosage is more important in determining clinical response to phenelzine in neurotic disorder than specific diagnosis or acetylator status. 36 references. (Author abstract modified)

**003642** Voelker, Sylvia Leah. Wayne State University **Methylphenidate in the treatment of hyperactivity in children: prediction of short-term response and multi-source assessment of long-term effects on behavior and academic achievement. (Ph.D. dissertation).** Dissertation Abstracts International. 40(11):5425-B, 1980. Ann Arbor, Univ. Microfilms No. 8010185, 180p., 1979.

The utility of an objective, multidimensional assessment device, the Personality Inventory for Children (PIC), for the prediction of initial methylphenidate response, and the behavioral and academic effects of the medication as reported by mothers and teachers after an average of 2 years of treatment, were investigated. Initial improvement ratings for 49 hyperactive Ss were made by two judges (in the areas of home, school, and academic achievement) using medical record information covering the first 2 months of stimulant treatment. Long-term medication effects were investigated through comparison of problem behavior checklists completed by mothers and teachers and objective achievement test results. It is concluded that the sensitivity of the PIC to differences between drug responders and nonresponders warrants further investigation, and that methylphenidate has little, if any, effect on the long-term behavioral and academic adjustment of treated children. (Journal abstract modified)

**003643** Wannamaker, Braxton B.; Morton, William A., Jr.; Gross, Alan J.; Saunders, Sharon. Dept. of Neurology, Medical University of South Carolina, Charleston, SC 29403 **Improvement in antiepileptic drug levels following reduction of intervals between clinic visits.** Epilepsia. 21(2):155-162, 1980.

A method of improving antiepileptic drug levels (AEDLs) in epileptic patients is described. Of 30 patients on stable drug regimens AEDLs were increased in 33% by decreasing clinic visit intervals from a mean of 3.4 months to 1.1 months. The testing situation was applied to patients who had AEDLs in the therapeutic range as well as those with one or more AEDLs below therapeutic range. In the latter group 73% of patients showed improvement in AEDLs. Although a less reliable parameter, verbally reported seizure frequencies were also improved. Overall, the reduction in clinic visit interval could be expected to yield improvement in 46% to 80%. These patients responded equally well to physician and nonphysician practitioners. It is concluded that this technique may be useful as an intervening measure for those patients who are noncompliant. 17 references. (Author abstract modified)

**003644** Wilsher, C.; Atkins, G.; Manfield, P. University of Aston, Birmingham, England **Piracetam as an aid to learning in dyslexia.** Psychopharmacology. 65(1):107-109, 1979.

Sixteen male dyslexic children were seen again when adults and matched with 14 student volunteers for a 21 day trial of piracetam. It was found, using a double-blind crossover technique, that dyslexics significantly increased their verbal learning by 15.0% and students by 8.6% (over and above their placebo increase). Regular medical, biochemical and hematological examinations performed during the study reveal no untoward effects of the trial drug. The administration of piracetam seems to have changed the dyslexic pattern of verbal learning. The gain in verbal learning and decrease in immediate forgetting would be most important in a remedial education setting. Although it is not a cure for dyslexics, piracetam appears to be a very useful aid to learning. Therapeutically, it would be important to establish the helpful effects of this drug on dyslexic children. 15 references. (Author abstract modified)

**003645** Zaccara, G; Galli, A. Neurophysiopathology Service, Dept. of Neurology, University of Florence, Florence, Italy **Effectiveness of simplified dosage schedules on the management of ambulant epileptic patients.** European Neurology. 18(5):341-344, 1979.

The effect of dosage schedules on plasma drug levels was evaluated in two groups of ambulant epileptic patients, whose treatment with diphenylhydantoin (DPH) or phenobarbital (PB) had been simplified by reducing the daily frequency of the dosage regimens. Although the patients received the same milligram per kilogram daily dosages of DPH or PB during the study, the mean plasma levels of the two drugs were significantly higher during the less frequent dosage regimens. The results obtained suggest that twice daily dosage schedules of DPH and once daily dosage schedules of PB are advantageous over more complicated dosage schedules resulting in a higher compliance among ambulant epileptic patients. 15 references. (Author abstract)

## 12 PSYCHOTOMIMETIC EVALUATION STUDIES

**003646** Kvalseth, Tarald O. Dept. of Mechanical Engineering, University of Minnesota, Minneapolis, MN 55455 **Human performance effects of marijuana.** International Journal of Rehabilitation Research. 2(4):529-531, 1979.

The effects of marihuana (approximately 6.5mg delta9-THC and 19.5 to 26mg delta9-THC) on motor control and complex reaction time were examined in six male student volunteers, all of whom were experienced marihuana users. Results indicated that marihuana caused a significant decrease in the movement time on the linear tapping task and significantly increased error rate. While having no effect on rotary movement time, marihuana did significantly increase error rate. For both motor control tasks, the task difficulty/dose level interaction was insignificant. Performance on the choice reaction task appeared to be unaffected by marihuana: drug conditions had no significant effects on reaction times. For all three tasks, performance varied considerably among subjects for the different experimental conditions. Perceived effects of the drug on performance also varied: half of the subjects reported feeling their performance unaffected; half felt the drug was detrimental to their performance. 3 references.

**003647** Markowitz, Robert Alan. Boston University Graduate School **The effects of phencyclidine on shock-maintained escape behavior in the rat: interaction with naloxone. (Ph.D. disserta-**

tion). Dissertation Abstracts International. 40(12):5629-B, 1980. Ann Arbor, Univ. Microfilms No. 8013211, 162p., 1980.

The effects of phencyclidine (PCP) on shock maintained escape behavior in the rat were investigated and the interaction of PCP with naloxone was examined. Results of the foot shock titration procedure (FST) demonstrate that PCP causes a dose related increase in sensitivity to the aversive stimulus and that the administration of naloxone potentiates this effect. In the acoustic startle response procedure, none of the treatments significantly altered the magnitude of Ss response to acoustic stimuli, indicating that the observed PCP-induced hypersensitivity (and possible hyperresponsivity) were specific for learned escape behavior from aversive stimuli, and were not reflected in similar changes in unlearned startle responses. Evidence that interactions between PCP and the endogenous opioid peptides, as well as other neurotransmitter systems, might mediate the analgesic, psychotomimetic, and other pharmacologic actions of PCP is cited. (Journal abstract modified)

**003648** Nahas, Gabriel G.; Paton, William D. M.; Braude, Monique; Jardillier, Jean Claude; Harvey, David J. no address **Marihuana: biological effects -- analysis, metabolism, cellular responses, reproduction and brain.** Advances in the biosciences, vols. 22 and 23. Oxford, Pergamon, 1979. 777 p.

Fifty-five readings on the biological effects of marihuana, given at the Satellite Symposium of the International Congress of Pharmacology held in Paris July 1978, are presented. Topics are consolidated under four headings: 1) quantification of cannabinoids and their metabolites in body fluids and tissues; 2) cannabinoids and cellular metabolism; 3) cannabis and reproduction; and 4) cannabis and the brain.

**003649** Sangiah, Subbiah; Gomez, Marcus V.; Domino, Edward F. Dept. of Physiology and Pharmacology, Purdue University, School of Veterinary Medicine, West Lafayette, IN 47907 **Accumulation of N,N-dimethyltryptamine in rat brain cortical slices.** Biological Psychiatry. 14(6):925-936, 1979.

The accumulation of radiolabeled N,N-dimethyltryptamine (14C-DMT) in rat brain cortical slices incubated at 37 C, is described. The process has many of the properties of an active uptake mechanism, being temperature sensitive, sodium dependent, saturable, and inhibited by metabolic inhibitors. Tryptamine derivatives were more effective than the catecholamines in competing for 14C-DMT accumulation. A number of pharmacologic drugs were inhibitors of 14C-DMT accumulation. In general, irrespective of pharmacologic class, the tertiary amines were more potent than the secondary or primary amines, although there were some exceptions. Most of the accumulated 14C-DMT was associated with the cytoplasmic fraction. Of the portion associated with the crude mitochondrial fraction, 54% was associated with nerve ending fractions. 32 references. (Author abstract modified)

**003650** Snyder, Solomon H. Dept. of Pharmacology and Experimental Therapeutics, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Phencyclidine.** Nature 285(5764):355-356, 1980.

Phencyclidine (PCP) use, effects, and mechanisms of effect are discussed. The similarity of PCP psychosis to schizophrenia is described. The behavioral action of the drug is examined by reviewing its history as a clinical anesthetic and then as a drug of widespread abuse. Recent research identifying PCP binding sites in the brain which may be unique PCP receptors is discussed, although drawbacks in the studies are noted. It is concluded that PCP may hold promise in clarifying abnormal brain function in schizophrenia. 13 references.

**003651** Strahlendorf, Jean Carol R. Philadelphia College of Pharmacy and Science **Mechanism of lysergic acid diethylamide influence upon optically evoked potentials. (Ph.D. dissertation).** Dissertation Abstracts International. 40(12):5631-B, 1980. Ann Arbor, Univ. Microfilms No. 8002709, 214p., 1978.

The effects of lysergic acid diethylamide (LSD) and serotonin (5-HT) in the ventrolateral geniculate nucleus (LGN) and the dorsal raphe nucleus on visual evoked potentials (VEP) were investigated in immobilized, artificially respired cats. Preliminary studies revealed that intravenous LSD elicited an increase in the amplitude of primary components of the VEP recorded from the occipital cortex. LSD augmentation may be representative of synaptic facilitation, suggesting increased reactivity of the visual pathway to afferent stimuli. Results suggest that the dorsal raphe nucelus, based upon its effects on VEPs, is an important site of action of LSD. Moreover, the failure of intraraphe LSD and 5-HT to elicit significant alterations of the LGN evoked potential may either reflect the resistant nature of evoked potentials recorded from direct relay centers such as LGN or the realization that an insufficient number of neuronal and synaptic events were modified in LGN to cause changes in gross thalamic waveforms. (Journal abstract modified)

## 13 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

**003652** Allen, Marcia Divoll; Greenblatt, David J.; Arnold, John D. Greenblatt: Clinical Pharmacology Unit, Massachusetts General Hospital, Boston, MA **Single- and multiple-dose kinetics of estazolam, a triazolo benzodiazepine.** Psychopharmacology. 66(3):267-274, 1979.

The pharmacokinetic properties of estazolam, a triazolo benzodiazepine hypnotic agent, were assessed in a series of healthy volunteers following single and multiple doses. After single oral doses of 2 to 16mg, peak plasma concentrations were reached within 6 hours. Values of elimination half-life ranged from 8.32 to 31.2 hours and did not vary significantly with dose. During 3 weeks of therapy, steady state plasma concentrations increased approximately in proportion to increasing doses, and accumulation was essentially complete within 3 days of each dose change. The mean observed dose ration was 1.84 which was slightly larger than the predicted ratio of 1.53. Exposure to multiple dose estrazolam therapy had no significant influence on the kinetics of a single dose of antipyrine, suggesting that estazolam neither stimulates nor inhibits enzyme activity in humans. It is concluded that the accumulation and elimination kinetics of estazolam can be classified as intermediate to those of the short acting (such as oxazepam) and the long-acting (such as diazepam) benzodiazepine derivatives. 22 references. (Author abstract)

**003653** Anderson, T. E.; Rutledge, L. T. Dept. of Zoology, University of Texas, Austin, TX 78712 **Inhibition in penicillin-induced epileptic foci.** Electroencephalography and Clinical Neurophysiology. 46(5):498-509, 1979.

To verify that recurrent inhibition is functionally decreased in the penicillin epileptic focus and to assess alternative sites for penicillin action, this phenomenon was investigated at the cellular level. Neurons were recorded extracellularly and response to stimuli was monitered throughout the transition from normal cortex to epileptogenic cortex. The results demonstrate a loss of effectiveness of recurrent inhibition measured at the pyramidal tract (PT) cell body in the penicillin focus. Further, the reduction in inhibitiory feedback occurs in conjunction with maintained or enhanced excitability of the neurons which are most likely candidates for inhibitory interneurons. It is concluded that penicillin most likely exerts its effect at the inhibitory synapses

onto PT cells in the cortex, thereby allowing excitatory input to have greater influence on neuronal firing. 21 references.

**003654** Arrigo, A.; Moglia, A.; Sandrini, G.; Pernice, A. Centro di Neurofisiologia Clinica dell'Universita, via Palestro 3, I-27100, Pavia, Italy **Present state of the quantitative analysis of the EMG related to drug effectiveness.** Pharmakopsychiatrie Neuro-Psychopharmakologie. 12(1):119-124, 1979.

Issues concerning quantitative analysis of EMG patterns reflecting the effectiveness of pharmacotherapeutic agents are reviewed, and the relationship between EEG and electromyographic (EMG) profiles of psychotropic drugs is discussed. Commonly used EMG techniques are described, along with the criteria for their use. It is contended that these techniques represent not only useful resources for documentation in hospitals or interpretation of neurophysiological mechanisms, but a method for evaluating the clinical effectiveness of pharmacologically active substances. Standardization of methods of analysis is cited as a major problem. Data are demonstrated which were obtained by interval analysis during the differential diagnosis of facial myokymia and during pharmacotherapy for this condition. 16 references. (Author abstract modified)

**003655** Bjerkenstedt, Lars; Gullberg, Bo; Harnryd, Christer; Sedvall, Goran. Laboratory of Experimental Psychiatry, Dept. of Psychiatry, Karolinska Hospital, S-104 01 Stockholm, Sweden **Relationships between clinical and biochemical effects of melperone and thiothixene in psychotic women.** Archiv fur Psychiatrie und Nervenkrankheiten. 227(3):181-192, 1979.

Clinical and biochemical effects of melperone and thiothixene were studied in women with psychoses of schizophrenic or paranoid type. The drugs were not found to differ in antipsychotic effect but thiothixene treatment caused greater elevation of homovanillic acid (HVA) and prolactin than melperone. The measures of dopaminergic activity did not correlate significantly with therapeutic outcome in either treatment group. Treatment with melperone, but not thiothixene, reduced 4-hydroxy-3-methoxyphenyl-ethylene glycol (MOPEG) levels, but only during thiothixene treatment was MOPEG reduction related to clinical improvement. In both treatment groups clinical improvement correlated significantly with an increase in the 5-hydroxy-3-indoleacetic acid/MOPEG ratio. Extrapyramidal side effects correlated negatively with HVA and HVA/MOPEG in the thiothixene, but not in the melperone group. It is concluded that there is no simple relationship between alteration of dopaminergic transmission and therapeutic outcome in drug treated psychotic patients. It is suggested that the balance of activity between central serotonin and norepinephrine systems should be considered in the mechanism of action of antipsychotic drugs and the pathophysiology of psychosis. 38 references. (Author abstract modified)

**003656** Eichelbaum, Michel; Kothe, K. W.; Hoffmann, F.; von Unruh, G. E. Dept. of Medicine, University of Bonn, D-5300 Bonn-Venusberg, Germany **Kinetics and metabolism of carbamazepine during combined antiepileptic drug therapy.** Clinical Pharmacology and Therapeutics. 26(3):366-371, 1979.

The kinetics of carbamazepine were investigated in epileptic patients treated wth 15N-carbamazepine in combination with primidone, phenytoin, phenobarbital, ethosuximide, or methsuximide. The 15N-carbamazepine plasma half-lives ranged from 5.0 to 13.6 hours (mean, 8.2 hours), which are appreciably shorter than those reported for chronic carbamazepine monotherapy. Between 32 and 61% of the dose administered was excreted in the urine as carbamazepine-trans-diol, 5.2 to 8.8% as 9-hydroxymethyl-10-carbamoyl acridone, 1 to 1.4% as 10,11-carbamazepine epoxide, and 0.5% as carbamazepine. Results indicate that the epoxide-diol pathway is induced during long-term treatment with carbamazepine and that carbamazepine metabolism can be further induced by concomitant administration of other anticonvulsant drugs. 24 references. (Author abstract modified)

**003657** Etevenon, P.; Pidoux, B. INSERM, 2 rue d'Alesia, F-75014 Paris, France **Progresses of statistical spectral analysis in pharmaco-electroencephalography.** Pharmakopsychiatrie Neuro-Psychopharmakologie. 12(1):102-110, 1979.

Statistical methodology for spectral analysis in pharmacoelectroencephalography is discussed and illustrated by analysis of right posterior hemispheric changes in EEGs of seven normal Ss, 14 hours after the administration of 5mg of nitrazepam. Fourier analysis briefly described, and the uses of an EEG data base of more than 220 FM recordings (90 minutes per recording) are discussed. It is noted that digital results from this EEG data base provide characteristic spectral parameters for further multivariate analyses. Other variables, such as drug plasma levels or clinical rating scales can also be added to the data base. The application of various EEG spectral analytic techniques to investigate CNS drug effects is discussed. 17 references. (Author abstract modified)

**003658** Fanciullacci, Marcello; Boccuni, Maria; Pietrini, Umberto; Sicuteri, Federigo. Dept. of Clinical Pharmacology, University of Florence, 50134 Florence, Italy **The naloxone conjunctival test in morphine addiction.** European Journal of Pharmacology. 61(3):319-320, 1980.

The response to conjunctival instillation of naloxone was compared in a 23-year-old morphine addict and three healthy control Ss. Naloxone induced a significant mydriatic effect in the morphine addict, but not in controls. The naloxone pupil test may provide a useful means of detecting morphine addiction. 5 references.

**003659** Faulkner, T. P.; McGinity, J. W.; Hayden, J. H.; Olson, D. A.; Comstock, E. G. College of Pharmacy, Ohio Northern University, Ada, OH **Pharmacokinetic studies on tolerance to multiple doses of sedative-hypnotics in a polydrug abuse population. II. Secobarbital-amobarbital.** Journal of Clinical Pharmacology. 19(10):605-616, 1979.

Tolerance of secobarbital/amobarbital (S-A) was examined in nine patients in an inpatient polydrug abuse clinic who considered S-A (Tuinal) their primary drug of abuse. These patients were able to tolerate a mean dose of S-A that was 58% higher than that tolerated by six control Ss. The elimination of secobarbital, but not amobarbital, was enhanced in the patient group. The apparent volume of distribution of secobarbital was greater in the patient group, but this difference was not significant. 30 references.

**003660** Fowler, Christopher J.; Oreland, Lars; Marcusson, Jan; Winblad, Bengt. Dept. of Pharmacology, University of Umea, S-901 87 Umea, Sweden **Titration of human brain monamine oxidase -A and -B by clorgyline and L-deprenil.** Naunyn-Schmiedeberg's Archives of Pharmacology. 311(3):263-272, 1980.

The interaction of clorgyline and L-deprenil with type-A and type-B of human brain monoamine oxidase (MAO) was studied. Both compounds inhibit cerebrocortical MAO in a manner consistent with a suicide inactivation of the enzyme. The interaction of clorgyline with the type-A enzyme appears to take place almost entirely at specific binding sites, and the conditions required for this inhibitor to titrate the concentrations of MAO-A have been elucidated. L-deprenil has also been used to titrate the concentration of type-B or MAO in cerebrocortical homogenates, but there is a considerable degree of nonspecific binding of this compound. The two inhibitors have been used to titrate

the concentrations of the two enzyme forms in frontal cortex homogenates from different age groups. There was a significantly higher MAO-B activity for the age range 73 to 95 years than for the age range 2 to 63 years. No significant differences between the two age groups were found for MAO-A. The activity of MAO-A in the samples correlated very well with the concentration of this enzyme form. Titration of the type-B enzyme with L-deprenil indicated an increased enzyme concentration with age, although other factors, such as the nonspecific binding of this compound, could contribute to this effect. 42 references. (Author abstract)

**003661** Ghose, Karabi. Lingfield Hospital School, St. Piers Lane, Lingfield, Surrey, RH7 6PN England **Assessment of peripheral adrenergic activity and its interactions with drugs in man.** European Journal of Clinical Pharmacology. 17(4):233-238, 1980.

The interactions of peripheral adrenergic activity and therapeutic drugs were assessed via tyramine, noradrenaline, and phenylephrine pressor response tests in patients suffering from affective disorders during various drug therapies or following electroconvulsive therapies (ECT). Tricyclic and related antidepressive drugs produced decreased tyramine sensitivity and increased noradrenaline sensitivity and blocked postsynaptic adrenergic receptors. However, the degree of blockade was variable, and some of the newer drugs, in the dosage used, were devoid of these peripheral interactions. No significant change in these pressor response tests were observed in patients who had three or more ECT treatments. On the other hand, patients treated with lithium carbonate for four or more weeks, had decreased phenylephrine and noradrenaline sensitivities, which were not associated with any change in tyramine sensitivity. Treatment with haloperidol for 48 hr decreased tyramine sensitivity two and a half fold, and is attributed to postsynaptic receptor blockade or inhibition of amine reuptake process or both. 26 references. (Author abstract modified)

**003662** Goldstein, L. Dept. of Psychiatry, CMDNJ, RMS. Box 101, Piscataway, NJ 08854 **A comparative study of the effects of imipramine in normal subjects: power spectrum vs. amplitude variance.** Pharmakopsychiatrie Neuro-Psychopharmakologie. 12(1):69-73, 1979.

A comparative study of the effects of imipramine on power spectrum and amplitude variances in normal Ss is described. EEG amplitudes from left and right occipital and temporal were cumulated over 60 successive 5 second intervals. With an acute oral dose of 50mg, imipramine was found to increase markedly (50% to 800%) the variances in both right and left occipital leads. The changes were less marked at temporal levels. However, they occurred in only 15 out of 30 male Ss. Placebo had no effect in either responders or nonresponders. Power frequency spectrum analysis revealed changes for delta, theta, and beta activities which were highly correlated with the increase of the variances. There was no correlation with the decrease of alpha activity, which was minimal. No significant correlations were found in nonresponders, and with placebo in both responders and nonresponders. 9 references. (Author abstract modified)

**003663** Greenblatt, David J.; Allen, Marcia Divoll; Harmatz, Jerold S.; Shader, Richard I. Division of Clinical Pharmacology, Box 10007, New England Medical Center, 171 Harrison Ave., Boston, MA 02111 **Diazepam disposition determinants.** Clinical Pharmacology and Therapeutics. 27(3):301-312, 1980.

Diazepam kinetics were assessed in young (21 to 37 years old) and elderly (61 to 84 year old) male and female Ss after a single 5 or 10mg i.v. dose. Based on total (bound and free) diazepam concentrations, the volume of distribution ranged from 0.7 to 4.7l/kg and was larger in older Ss and in women. Clearances of total diazepam were nearly identiical in young and old women, but clearance was higher in young men than in old men. The unbound fraction of diazepam in plasma was greater in the elderly than in the young and did not vary with sex. Clearance of unbound diazepam tended to be higher in females than in males of both age groups and was higher in the young than in the elderly of both sexes. Smoking was associated with higher clearance values, particularly among young Ss. 36 references. (Author abstract modifed)

**003664** Halliday, Roy Arthur. University of California, San Francisco **The effects of methylphenidate dosage on the visual evoked potential, heart rate and reaction time in hyperactive children. (Ph.D. dissertation).** Dissertation Abstracts International. 40(12):5859-B, 1980. Ann Arbor, Univ. Microfilms. No. 8012822, 79p., 1980.

The effects of methylphenidate (Ritalin) dosage on concurrent measures of heartrate (HR), averaged visual evoked potentials (VEP) and reaction time (RT) were investigated in 29 hyperactive children during four different sessions. HR and VEPs were recorded under an active and a passive attention condition, 60 min following ingestion of placebo or an oral dose of methylphenidate. Results indicate that stimulant dosage produced several different dose response curves. RT measures and mean HR increased up to the .33mg/kg dose and then showed nonfurther changes with increasing dosage. The amplitude of N160 and correlations between RT and amplitude of the N160 component increased at the .16 and .33 dosages and declined at higher doses. The amplitude of P230 was larger in older children, while the latency of this component occurred earlier in the active attention condition. (Journal abstract modified)

**003665** Hjorth, Bo. Siemens-Elema AB, Dept. EU-GI, S-0171 95 Solna, Sweden **Mutichannel EEG preprocessing: analogue matrix operations in the study of local effects.** Pharmakopsychiatrie Neuro-Psychopharmakologie. 12(1):111-118, 1979.

The use of analogue matrix operations in the study of local EEG effects of psychotropic drugs is discussed. An approach based on simple matrix algebra concepts can be used to comprehend the potential field in the scalp as one entity, rather than observing single potential differences on the surface. It is demonstrated that existing methods of deriving EEG (bipolar, referential, etc.) can be clearly formulated using such concepts, which can also include interpretive operations. The simplest possible interpretive model utilizes the fact that derived signals refer to a given pattern of electrodes on a surface. This model provides the basis for source derivation, as previously described (Hjorth, 1976). The interpretive model may be further developed to include the transfer of electrical potentials from a driving potential distribution on a subsurface level in a conductive body by the resultant distribution on the surface. By expressing this transfer function as a matrix operator and performing a matrix inversion, coefficients can be determined for a simple analogue network which is capable of deriving on-line signals representative of a focal plane below the surface, thus providing a corresponding improvement in spatial resolution. 3 references. (Author abstract modified)

**003666** Janowsky, David; Judd, Lewis; Huey, Leighton; Roitman, Norton; Parker, Donal. Dept. of Psychiatry, University of California at San Diego, Medical School, La Jolla, CA 92093 **Naloxone effects on serum growth hormone and prolactin in man.** Psychopharmacology. 65(1):95-97, 1979.

The effects of naloxone hydrochloride on serum growth hormone and prolactin in man were explored. Endogenous and exogenous opiate-like compounds have been found to cause in-

creased serum growth hormone and prolactin levels in animals, and, in some cases, humans. Naloxone, a relatively specific narcotic antagonist, decreases serum prolactin and growth hormone levels in animals. Naloxone (20mg i.v.) did not significantly alter serum prolactin levels and, minimally but not significantly, increased growth hormone levels in humans to whom it was administered. Possibilities which may be pertinent in explaining the discrepancy between the findings in human and animal models are discussed. 9 references. (Author abstract modified)

**003667** Johnson, R. F.; Schenker, S.; Roberts, R. K.; Desmond, P. V.; Wilkinson, G. R. Wilkinson: Veterans Administration Hospital, Nashville, TN **Plasma binding of benzodiazepines in humans.** Journal of Pharmaceutical Sciences. 68(10):1320-1322, 1979.

Plasma binding of chlordiazepoxide, diazepam, lorazepam, and oxazepam was determined by equilibrium dialysis in 20 male, healthy volunteers (25 to 86 years old). A wide range of binding was observed; the free fraction varied twofold for lorazepam, fourfold for chlordiazepoxide and diazepam, and more than 20 fold for oxazepam. No significant linear relationships were observed between the degree of binding and age, serum albumin, or total protein for any of the drugs, but a correlation was observed for the extent of binding of the four drugs. 10 references. (Author abstract modified)

**003668** Kalofoutis, A.; Lekakis, J.; Koutselinis, A. Dept. of Biological Chemistry, University of Athens School of Medicine, Goudi (609), Greece **Effects of delta9-THC on human platelet phospholipids.** Pharmacology Biochemistry and Behavior. 12(5):697-699, 1980.

Platelet lipids were studied in chronic hashish users before and after they smoked delta-tetrahydrocannabinol. Results revealed significant decreases in phosphatidylcholine and phosphatidylinositol and a significant increase in phosphatidylethanolamine after smoking the drug. No significant differences in total lipids, total phosphoplipids, and individual phosphalipids were found between the chronic hashish users and controls before smoking or before and after smoking tobacco. 23 references. (Author abstract modified)

**003669** Krebs, Eva; Roubicek, J. Psychiatric Clinic Wil, CH-9500 Wil, Switzerland **EEG and clinical profile of a synthetic analogue of methionine-enkephalin -- FK 33-824.** Pharmakopsychiatrie Neuro-Psychopharmakologie. 12(1):86-93, 1979.

An EEG and clinical profile of a synthetic analogue of methionine-enkephaline (FK 33-824) is presented. EEG investigation of FK 33-824 in 20 normal volunteers (compared with placebo in eight of them) indicated typical changes in electrical activity in the conventional description and a simultaneous spectral analytic evaluation, with an increase in alpha and beta activity, with decrease in slow-waves. The changes after FK 33-824 differ from placebo changes and from the well known changes seen after opioid alkaloids. In view of this cerebral action of FK 33-824 and of the possible involvement of endorphins in mental disease, clinical trials were initiated. In a pilot study, intramuscular FK 33-824 induced a short-term improvement in the symptoms of four of six psychotic patients. 14 references. (Author abstract modified)

**003670** Lees, A. J.; Lander, C. M; Stern, G. M. National Hospital, Queen Square, London WC1N 3BG **Tiapride in levodopa-induced involuntary movements.** Journal of Neurology, Neurosurgery, and Psychiatry. 42(4):380-383, 1979.

Tiapride, a substituted benzamide derivative closely related to metoclopramide, reduced levodopa-induced peak dose involuntary movements in 16 patients with idiopathic Parkinson's disease. However, an unacceptable increase in disability from Parkinsonism with aggravation of end of dose akinesia led to its cessation in 14 patients. Tiapride had no effect on levodopa-induced early morning and the notion that levodopa-induced dyskinesias are caused by overstimulation of a separate group of dopamine receptors. 18 references. (Author abstract)

**003671** Magnussen, I.; Oxlund, H. R. W.; Alsbirk, K. E.; Arnold, E. Biological Dept. , Dumex Ltd., DK-2300 Copenhagen, Denmark **Absorption of diazepam in man following rectal and parenteral administration.** Acta Pharmacologica et Toxicologica. 45(2):87-90, 1979.

Serum concentrations of diazepam and N-desmethyldiazepam were measured in six adult patients following administration of 10mg diazepam in solution by the rectal, intravenous, and intramuscular routes. Maximum serum concentrations of 121 to 200ng/ml were recorded 10 to 20 minutes after the rectal instillation. In contrast, levels rose slowly and irregularly following intramuscular injection, reaching a maximum of 62 to 186ng/ml in 1 to 24 hours. The bioavailability of diazepam given by rectal instillation was only about half that achieved with intravenous injection. It is concluded that diazepam administration by rectal tube is a useful alternative to oral or intramuscular administration when rapid onset of drug effect is desired and when intravenous administration is not practical. 8 references. (Author abstract modified)

**003672** Mantovani, John; DeVivo, Darryl C. DeVivo: Neurological Institute, 710 West 168th Street, New York, NY 10032 **Effects of taurine on seizures and growth hormone release in epileptic patients.** Archives of Neurology. 36(11):672-674, 1979.

The effects of taurine on seizures and growth hormone release in epileptic patients were investigated. Oral taurine at doses of 375 to 8,000mg/day was administered to six patients with mixed seizure disorders refractory to standard anticonvulsant treatment. No improvement in seizure control was observed. During taurine tolerance testing, a substantial rise in plasma growth hormone concentration was noted in four of the six patients. Mean baseline concentrations were increased following taurine administration. Cerebrospinal fluid homovanillic acid (HVA) concentration was also noted to be higher in two of three patients 2 weeks after initiation of taurine. Initial HVA concentrations increased significantly. The possible effect of taurine on central dopaminergic mechanisms is discussed. 11 references. (Author abstract modified)

**003673** Marttila, Reijo J.; Rinne, Urpo K. Dept. of Neurology, University of Turku, SF-20520 Turku 52, Finland **Changing epidemiology of Parkinson's disease: predicted effects of levodopa treatment.** Acta Neurologica Scandinavica. 59(2/3):80-87, 1979.

The prediction that levodopa treatment reduces the excess mortality due to the Parkinson's disease, and that it affects the equilibrium state of the epidemiology of the disease was investigated. The predicted increase in the prevalence of the disorder was computed according to the mortality pattern expected in the general population and in a pattern that is 1.5 times greater. The predicted increase in disease duration is 6.3 or 3.2 years, while the proportional increase in prevalence is 1.8 and 1.4, respectively. The results indicate that there will be an increase of patients with long-term levodopa treatment difficulties and with Parkinson's symptoms not treatable with the drug (e.g. dementia). This warrants research into new treatment approaches. 27 references. (Author abstract modified)

**003674** Meinhold, Jane M.; Spunt, Avery L.; Trirath, Chantima. Dept. of Pharmacy Practice, University of Illinois College of Pharmacy, Chicago, IL **Bioavailability of lithium carbonate:**

**in vivo comparison of two products.** Journal of Clinical Pharmacology. 19(11 and 12):701-703, 1979.

The bioavailability of two lithium carbonate products (Philips Roxane and Smith Kline and French Laboratories) was investigated in 10 healthy, normal volunteers. Three of the volunteers had distinctly greater values with Smith kline and French lithium, and four volunteers had distinctly greater AUC values with Philips Roxane lithium. Results indicate that there are no significant differences in bioavailability of the two brands, but that individual differences may exist. 6 references.

**003675** Mellstrom, Britt; Bertilsson, Leif; Traskman, Lil; Rollins, Douglas; Asbert, Marie; Sjoqvist, Folke. Dept. of Clinical Pharmacology, Huddinge Hospital, S-141 86 Huddinge, Sweden **Intraindividual similarity in the metabolism of amitriptyline and chlorimipramine in depressed patients.** Pharmacology. 19(5):282-287, 1979.

Steady-state plasma levels of amitriptyline (AT), chlorimipramine (CI), and their demethyl metabolites were determined in 15 patients treated with AT and CI. High performance liquid chromatography revealed a five fold interindividual variation in plasma levels of all four compounds. A significant correlation was found between the reciprocal plasma levels of CI and demethylchlorimipramine and between AT and nortriptyline. The reciprocal plasma levels of the parent compounds were closely correlated, as were those of the demethyl metabolites. Results indicate that similar factors control the plasma levels of AT and CI during treatment and that similar enzymes may be involved in the metabolism of the two drugs. 24 references. (Author abstract modified)

**003676** Meltzer, Herbert L. Dept. of Biochemistry, College of Physicians and Surgeons, Columbia University, New York, NY 10032 **The effect of ruthenium red and NEM on lithium efflux from human erythrocytes.** Psychopharmacology. 64(1):25-30, 1979.

The effects of N-ethylmaleimide (NEM) and ruthenium red, each of which inhibits the calcium (Ca) pump, on lithium (Li) efflux from human erythrocytes were examined. The Li pump intact human erythrocytes, which has previously been shown to be repressed following lithium carbonate ingestion in manic-depressive subjects, was found to be inhibited selectively by NEM and ruthenium red. It is proposed that active Li efflux is linked to the concurrent operation of the Ca pump. This inference is strongly supported by previous studies of effects of NEM and ruthenium red on the Ca pump. It is possible that Li transport may occur as a consequence of binding to Ca ATPase sites or that the Li ion, whose ionic radius is similar to that of Mg and whose charge density is similar to that of Ca may participate as a surrogate in the Ca ATPase system. 31 references. (Author abstract modified)

**003677** Modai, I.; Apter, A.; Golomb, M.; Wijsenbeek, H. Geha Psychiatric Hospital, Beilinson Medical Center, Petah-Tikva, Israel **Response to amitriptyline and urinary MHPG in bipolar depressive patients.** Neuropsychobiology. 5(4):181-184, 1979.

The hypothesis that urinary 3-methoxy-4-hydroxypenylglycol (MHPG) levels provide a predictor of response to therapy in depressed patients was tested with 15 elderly bipolar depressives. Their depressive state was estimated by the Hamilton Depressive Scale and their urinary MHPG levels were simultaneously measured before and after 5 weeks of amitriptyline therapy. When amitriptyline responders were compared to nonresponders by parametric techniques, it was found that responders excreted significantly higher mean MHPG levels before the treatment than the nonresponders. During treatment, MHPG levels rose significantly in both groups. 13 references. (Author abstract)

**003678** Muller, Walter E.; Wollert, Uwe. Pharmakologisches Institut der Universitat Mainz, Obere Zahlbacher Strasse 67, D-6500 Mainz, Germany **Human serum albumin as a 'silent receptor' for drugs and endogenous substances.** Pharmacology. 19(2):59-67, 1979.

Properties of the specific drug binding sites of human serum albumin (HSA), which acts as a secondary or silent receptor for drugs and endogenous substances, are reviewed. The actual number of high affinity drug binding sites of HSA appears to be small, but each of these sites binds several drugs of very different chemical and pharmacological properties with relative high affinity. The most striking example of a receptor-like specific binding site of the HSA molecule is the indole binding site, which binds L-tyrptophan, other indole compounds, and tranquilizers of the benzodiazepine group. 69 references. (Author abstract modified)

**003679** Nakano, Shigeyuki; Ogawa, Nobuya; **Kawazu, Yusuke.** Dept. of Pharmacology, Ehime University School of Medicine, Shigenobu-Cho, Onsen-Gun, Ehime-Ken, 791-02, Japan **Influence of neuroticism on oral absorption of diazepam.** Clinical Pharmacology and Therapeutics. 27(3):370-374, 1980.

The absorption of a single 5mg oral dose of diazepam was studied in 24 young male Ss, half with high neuroticism (HN) scores on the Maudsley Personality Inventory and half with low neurotocism (LN) scores. The mean plasma concentration for diazepam was significantly higher in HN Ss than in LN Ss 1.5 hours after drug administration. Diazepam plasma levels did not differ between groups when the drug was administered directly into the duodenum through a tube. No clear relationship between plasma drug concentrations and sedative effects was observed. Results suggest that the rate of diazepam absorption from the gastrointestinal tract is faster in HN Ss than in LN Ss due to a faster gastric emptying time in HN Ss. 12 references. (Author abstract modified)

**003680** Ochs, Hermann R.; Greenblatt, David J.; Allen, Marcia Divoll; Harmatz, Jerold S.; Shader, Richard I.; Bodem, Gunther. Greenblatt: Clinical Pharmacology Unit, Massachusetts General Hospital, Boston, MA 02114 **Effect of age and Billroth gastrectomy on absorption of desmethyldiazepam from clorazepate.** Clinical Pharmacology and Therapeutics. 26(4):449-456, 1979.

The absorption of desmethyldiazepam (DMDZ) following a single 20mg oral dose of its precursor, clorazepate (CZP) dipotassium, was studied in six healthy young men (mean age, 24 years), eight older men (mean age, 66.5 years) with no gastrointestinal disease, and 10 patients (mean age, 56 years) who had undergone Billroth gastrectomy at least 2 years before. Absent or impaired gastric acid secretion was documented in of the 10 postgastrectomy patients. Results showed that variability in DMDZ absorption was associated with age rather than with gastrectomy or acid secretion status. The appearance of DMDZ in the systemic circulation was reduced in both groups of older men, possibly as a result of reduced conversion of CZP to DMDZ or increased distribution of DMDZ in the elderly. Normal gastric acidity was not essential for absorption of DMDZ derived from CZP. 26 references. (Author abstract modified)

**003681** Pataky, I. National Institute of Neurology and Psychiatry, Budapest, Hungary **Therapy of depressions, biochemical aspects of pathogenesis.** Therapia Hungarica. 27(4):161-165, 1979.

Findings on the biochemical aspects of the pathogenesis of depression are reviewed. The effects of the tricyclic antidepressants on depressive patients and healthy individuals are summarized. The mechanism of action of tricyclic antidepressants is believed to involve receptor reactivation. The tricyclics may also cause a deficiency of impulse transmitter molecules in the presynaptic cells and set off a feedback mechanism that increases the activity of the enzymatic chain. It has also been hypothesized that monoamine oxidase inhibitors result in an abundance of transmitter molecules. These notions about antidepressant mechanisms of action have been explored as potential clues to the pathogenesis of depression. 17 references.

**003682** Patel, Indravadan H.; Levy, Rene H.; Cutler, Ralph E. Levy: Dept. of Pharmaceutical Sciences, BG-20, School of Pharmacy, University of Washington, Seattle, WA 98195 **Phenobarbital-valproic acid interaction.** Clinical Pharmacology and Therapeutics. 27(4):515-521, 1980.

Subchronic treatment with valproic acid inhibited the metabolism of phenobarbital in normal male Ss. In Ss treated with valproate, phenobarbital half-life rose from 96 to 142 hours. Plasma and metabolic clearances decreased, but renal clearance was unchanged. The fraction of the dose excreted unchanged rose from 0.22 to 0.33. 27 references. (Author abstract modified)

**003683** Pentikainen, Pertti J.; Neuvonen, P. J.; Jostell, K.-G. Second Dept. of Medicine, University of Helsinki, Haartmaninkatu 4, SF-00290 Helsinki 29, Finland **Pharmacokinetics of chlormethiazole in healthy volunteers and patients with cirrhosis of the liver.** European Journal of Clinical Pharmacology. 17(4):275-284, 1980.

The pharmacokinetics of chlormethiazole after oral and intravenous administration were studied in six healthy volunteers and eight patients with alcoholic cirrhosis of the liver. Plasma concentration time curves after the intravenous infusion were adequately described by two or three compartment open models both in healthy volunteers and in the patients. Based on the areas under the plasma concentration time curves, the systemic bioavailability of oral chlormethiazole was about 10 times greater in the patients than in healthy control Ss. The elimination of chlormethiazole was relatively less retarded in the patients, as indicated by a decrease of about 30% in its plasma clearance. The increased bioavailability of oral chlormethiazole is attributed to impaired first pass metabolism in the cirrhotic liver. A considerable reduction in dose seems to be indicated if oral chlormethiazole is used in patients with advanced cirrhosis of the liver. 28 references. (Author abstract modified)

**003684** Potter, William Z.; Muscettola, Giovanni; Goodwin, Frederick K. Clinical Psychobiology Branch, National Institute of Mental Health, 9000 Rockville Pike, Building 10, Room 4S239, Bethesda, MD 20014 **Binding of imipramine to plasma protein and to brain tissue: relationship to CSF tricyclic levels in man.** Psychopharmacology. 63(2):187-192, 1979.

The possible clinical significance of the plasma protein binding of tricyclic antidepressants in humans was evaluated using imipramine (IMI). Using equilibrium dialysis, the in vitro binding of IMI to plasma was compared to that of brain tissue. Cerebrospinal fluid (CSF) IMI was used as an independent measure of free drug in the central nervous system. Intrinsic metabolic clearances were calculated on the basis of steady-state plasma IMI concentrations. There were three significant results: 1) variations in plasma binding were not great; 2) plasma protein binding did not limit the entry of IMI into the CSF; 3) variations in metabolism accounted for almost all variations in CSF concentrations of drug. It is concluded that measurement of free tricyclic antidepressant is not indicated in studies of clinical efficacy. 30 references. (Author abstract)

**003685** Pritchard, James Frederick. Pennsylvania State University **Quantitative studies on propranolol metabolism in rat and man. (Ph.D. dissertation).** Dissertation Abstracts International. 41(1):152-B, 1980. Ann Arbor, Univ. Microfilms No. 8015832, 295p., 1980.

The metabolism of propranolol, a widely used beta-adrenergic blocking agent, was studied quantitatively in both rat and man. The development of sensitive methodology for measuring propranolol and most of its known metabolites in urine, plasma, and tissue preparations is described. Urinary profiles of propranolol metabolites in both rat and man following repetitive propranolol treatment were altered and intrinsic clearance in man was reduced, consistent with an inhibition of first choice metabolic pathways such as hydroxylation. The demonstration of specific inhibition by propranolol of its own metabolism probably mediated through covalent binding by ametabolite to the very enzymatic site that produced the reactive species as a novel mechanism for the inhibition of drug metabolism. (Journal abstract modified)

**003686** Propping, Peter; Friedl, Waltraut Institut fur Humangenetik, Universitat Heidelberg, Neuenheimer Feld 328, D-6900 Heidelberg, Germany **Genetic influences on pharmacodynamic properties of psychotropic drugs.** Pharmacology. 19(1):1-4, 1979.

Hereditary interindividual differences in pharmacodynamic response to psychotropic drugs are discussed. The differential effects of psychotropic drugs on the EEG apparently reflect genetic differences in brain function. Lithium transport across the erythrocyte membrane also exhibits large interindividual differences that have a genetic basis and may indicate a link between lithium transport and manic-depressive psychosis. 23 references. (Author abstract modified)

**003687** Quik, M.; Spokes, E. G.; Mackay, A. V. P.; Bannister, R. Mackay: MRC Neurochemical Pharmacology Unit, Cambridge University, Hills Road, Cambridge CB2 2QD, England **Alterations in (3H)spiperone binding in human caudate nucleus, substantia nigra and frontal cortex in the Shy-Drager syndrome and Parkinson's disease.** Journal of the Neurological Sciences. 43(3):429-437, 1979.

Tritiated spiperone binding was examined in the caudate nucleus, substantia nigra, and frontal cortex of patients with Parkinson's disease or the Shy-Drager syndrome and in control Ss. Scatchard analysis showed that the maximal number of binding sites (Bmax) was similar for all three groups in the caudate, but was reduced by about 60% in the substantia nigra of both patient groups. The dissociation constant was similar in all three groups in substantia nigra, but was increased in the caudate nucleus of patients with Shy-Drager syndrome. Binding characteristics of frontal cortex were similar in all three groups. These findings suggest a loss of dopamine receptor sites in the substantia nigra of patients with Parkinson's disease or Shy-Drager syndrome and a reduced affinity of dopamine receptor sites in the caudate nucleus in the Shy-Drager syndrome. 23 references. (Author abstract modified)

**003688** Rapoport, Judith L.; Tepsic, Patricia N.; Grice, Janice; Johnson, Christine; Langer, Dennis. Biological Psychiatry Branch Intramural Research Program, NIMH, Bldg. 10, Rm. 3N204, 9000 Rockville Pike, Bethesda, MD 20205 **Decreased motor activity of hyperactive children on dextroamphetamine during active gym program.** Psychiatry Research. 2(3):225-229, 1980.

The motor activity of 10 hyperactive 7 to 11-year-old boys was measured during eight 1 hour active gym classes after children received either dextroamphetamine or placebo elixir before each class in a double-blind design. The program for each of the classes was participation in the active sports; the task throughout each hour was to play vigorously and continuously. The boys' mean hourly activity following amphetamine was slightly but significantly less than that following placebo. This finding is contradictory to the hypothesis that improved attention to an active task on stimulant would result in increased motor activity, and suggests the possibility of an independent direct effect of amphetamine on the motor system. 13 references. (Author abstract)

**003689** Rehavi, Moshe; Paul, Steven M.; Skolnick, Phil; Goodwin, Frederick K. Paul: Clinical Psychobiology Branch, NIMH, 9000 Rockville Pike, Bethesda, MD 20205 **Demonstration of specific high affinity binding sites for (3H) imipramine in human brain.** Life Sciences. 26(26):2273-2279, 1980.

High affinity binding sites for (3H) imipramine were characterized in membranes prepared from human brain. The binding of (3H) imipramine was found to be saturable, reversible, and inhibited by pharmacologically active tricyclic antidepressants. Other psychoactive compounds as well as most neurotransmitter substances were ineffective in inhibiting (3H) imipramine binding at concentrations up to 10microM. The hypothalamus was found to contain a relatively high density of these binding sites and is enriched approximately four fold when compared to cerebral and cerebellar cortex. A very good correlation was found between the abilities of a series of clinically active tricyclic antidepressants in displacing specifically bound (3H) imipramine from human brain and platelet membranes, suggesting that the binding sites from these two tissues are very similar. 16 references. (Author abstract modified)

**003690** Reisine, Terry David. University of Arizona **Neuroleptic receptors: their characteristics in the mammalian central nervous system and their alteration in human neuropsychiatric disorders. (Ph.D. dissertation).** Dissertation Abstracts International. 40(9):4251-B, 1980. Ann Arbor, Univ. Microfilms No. 8005518, 145p., 1979.

The characteristics of CNS neuroleptic receptors were investigated in rats, and alterations of these neuroleptic receptors by human neuropsychiatric disorders were examined in schizophrenic, Parkinson's disease, and Huntington's disease patients. It was found the (3H)spiroperidol binding has a distinct regional distribution in rat and human brain. The neostriatum has the highest binding, followed by the mesolimbic region, cerebral cortex, and hypothalamic regions. The cerebellum has the lowest level of specific binding. Among schizophrenic patients, (3H)spiroperidol binding was elevated in the neostriatum yet unaltered in the frontal cortex as compared to controls. The density of opiate receptors, however, was reduced in the caudate nucleus of schizophrenic patients, yet unaltered in the putamen and frontal cortex of these brains. (Journal abstract modified)

**003691** Rieger, H.; Krieglstein, J.; Schultz, H. Psychiatrische Universitatsklinik, Langenbeckstrasse 1, D-6500 Mainz, Germany **Amplitude histography of the EEG in psychopharmacological research.** Pharmakopsychiatrie Neuro-Psychopharmakologie. 12(1):94-101, 1979.

Amplitude histography and interval histography are comparatively evaluated as EEG analysis techniques in psychopharmacological research, and the EEG drug effects of chlorpromazine and five of its metabolites, imipramine, and imipramine-N-oxide are described. Results include: 1) some drugs are well characterized by their EEG effects and can be easily discriminated from control experiences and less active substances; 2) the discriminating power of amplitude analysis is nearly equivalent to that of frequency measures. In particular, the standard amplitude (standard deviation of the amplitude histogram) and the excess of kurtosis are sensitive indicators of EEG drug effects; the third central momemt (skewness) is less significant, but can be of interest in particular cases; and 3) certain transient but important EEG events, such as spikes, sharp waves or high voltage theta groups, cause a marked deviation from a gaussian amplitude distribution (positive excess of kurtosis); these EEG phenomena are not reflected adequately by analysis methods in the time or frequency domain. 22 references. (Author abstract modified)

**003692** Roccatagliata, Giuseppe; De Cecco, L.; Rossato, P.; Albano, C. Aiuto Clinica delle Malattie Nervose e Mentali dell'Universita di Genova, Via A. De Toni, 5, I-16132 Genoa, Italy **Trazodone intravenously administered and plasma prolactin levels.** International Pharmacopsychiatry. 14(5):260-263, 1979.

Plasma prolactin levels during intravenous continuous (75 min) trazodone infusion were evaluated in 10 female psychiatric inpatients. Although the modifications were not statistically significant, a slight decrease of plasma prolactin levels was noted. Results suggest that trazodone has no remarkable effect on hypothalamic function. Findings are discussed in relation to experimental evidence that raised plasma prolactin levels promote induction of mammary tumors in the rat. 9 references. (Author abstract modified)

**003693** Rommelspacher, Hans; Honecker, Henning; Barbey, Maria; Meinke, Bernhard. Institut fur Neuropsychopharmakologie der Freien Universitat Berlin, Ulmenallee 30, D-1000 Berlin 19, Germany **6-Hydroxytetrahydronorharmane (6-hydroxy-tetrahydro-beta-carboline), a new active metabolite of indole-alkylamines in man and rat.** Naunyn-Schmiedeberg's Archives of Pharmacology. 310(1):35-41, 1979.

Following oral administration of 300mg L-5-hydroxytryptophan to four male volunteers, the glucuronic acid conjugate of 6-hydroxy-tetrahydronorharmane (6-OH-THN) was found in the urine. The metabolite was also detected in rat forebrain. In behavioral experiments in mice, 6-OH-THN induced hypothermia and catalepsy and reduced motility and nociception in a dose dependent manner. It is concluded that 6-OH-THN is a biologically active substance which may act as a modulator of neuronal mechanisms. 19 references. (Author abstract modified)

**003694** Routledge, P. A.; Kitchell, B. B.; Bjornsson, T. D.; Skinner, T.; Linnoila, M.; Shand, D. G. Shand: Box 3813, Division of Clinical Pharmacology, Duke University Medical Center, Durham, NC 27710 **Diazepam and N-desmethyldiazepam redistribution after heparin.** Clinical Pharmacology and Therapeutics. 27(4):528-532, 1980.

The effect of heparin on circulating concentrations of diazepam and its active metabolite, N-desmethyldiazepam, were studied. In normal Ss given heparin 3 hours after oral administration of 10mg diazepam, free drug levels rose with no change in blood or total plasma drug levels. Results suggest that factors other than simple plasma binding displacement are involved in the interaction of heparin and diazepam. 17 references. (Author abstract modified)

**003695** Rubin, Robert T.; Hays, Sally E. B-4 Neuroendocrine Lab., Harbor General/UCLA Medical Center, Torrance, CA 90509 **Variability of prolactin response to intravenous and intramuscular haloperidol in normal adult men.** Psychopharmacology. 61(2):17-24, 1979.

Serum prolactin (PRL) concentrations were monitored in seven normal adult men for 1 hour before and 7 hours after i.v. and i.m. injection of 0.25mg and 0.50mg haloperidol. The magnitude of the PRL response was dose related but quite variable across subjects. The patterns of PRL secretion over the 7 hour postinjection period also varied greatly among the subjects. Differences in serum haloperidol concentrations accounted for 88% of the variability in the magnitude of the PRL response to the 0.5mg i.m. haloperidol dose, but only accounted for 60% of the PRL variability following the 0.5mg i.v. dose. The pattern of haloperidol disappearance from serum was similar across the seven subjects and thus unrelated to the variable patterns of PRL response. 37 references. (Author abstract)

**003696** Saito, Masami. Dept. of Neuropsychiatry, Kansai Medical University, Fumizono-cho, Moriguchi, Osaka 570, Japan **Drug-induced EEG changes studied on two-dimensional rectangular coordinates using principal component analysis.** Pharmakopsychiatrie Neuro-Psychopharmakologie. 12(1):59-68, 1979.

Computerized EEG measurements collected from normal volunteers in single dose oral administration trials with diazepam, imipramine, and inert placebo and from patients with schizophrenia, depression, and epilepsy were processed using principal component analysis, and subject, drug, and time related changes in EEG were examined. With the results obtained, structure vector profiles, frequency band dispersions, and time course of factor scores were tentatively diagrammed. Of the three diagrams, factor score appears to be useful in displaying EEG changes as a locus on the rectangular coordinates without essential loss of information. By means of this diagramming technique, the loci generated by the factor score point show the different EEG changes induced by inert placebo, imipramine, and diazepam in the normal volunteer study. In patients with schizophrenia, treated factor score diagram with chlorpromazine shows the importance of distance, in those treated with haloperidol, direction is important, and in those treated with perphenazine, the different locations of the point are significant in distinguishing therapy responsive from therapy resistant cases. In cases of depression, the difference of displacement for the first three hours appears to be a predictor of clinical outcome regardless of the drugs used. Also, the factor score point runs between the second and fourth quadrants in the therapy resistant cases. In the influence of antiepileptic drugs a relatively small displacement was seen for the first three hours and a greater displacement was common for the first week; this appears to be due to the gradual rise in serum concentration of the drug, because fall in concentration caused a retrogression of the factor score point on the coordinates. The usefulness of principal component analysis of computerized EEG data is discussed and compared with that of factor analysis and cluster analysis for processing itemized clinical evaluations with the rating scale. 9 references. (Author abstract modified)

**003697** Saletu, B.; Grunberger, J. Psychiatrische Universitatsklinik, Lazarettgasse 14, A-1097, Vienna, Austria **Evaluation of pharmacodynamic properties of psychotropic drugs: quantitative EEG, psychometric and blood level investigations in normals and patients.** Pharmakopsychiatrie Neuro-Psychopharmakologie. 12(1):45-58, 1979.

The evaluation of pharmacodynamic properties of psychotropic drugs via quantitative EEG, psychometric test, and blood level data is discussed, and an evaluation study of a new pyridodiazepine, lopirazepam (D 12524) is described. Psychometric tests employed included evaluation of attention, concentration, psychomotor activity, critical flicker frequency, reaction time, Archimedean spiral, mood, and affectivity. Results indicate that short-term drug effects in the EEG of normal volunteer Ss are predictive of EEG and clinical effects in patients. Pharmaco EEG profiles of lopirazepam were found to be similar in normal Ss and alcoholic patients with anxiety syndrome. Quantitative EEG changes during treatment were found to be correlated with clinical improvement or deterioration, and the possibility that single dose effects on EEG may eventually be utilized to predict therapeutic outcome is noted. Relationships between blood level, quantitative EEG and psychometric changes after administration of phentermine and oxazepam are described and discussed. 37 references. (Author abstract modified)

**003698** Schultz, Joachim. Pharmazeutisches Institut der Universitat, Morgenstelle 8, D-7400 Tubingen, Germany **Psychotropic drugs and cyclic AMP in the brain.** Pharmacology. 18(2):57-63, 1979.

The role of the cyclic AMP generating system in the mechanism of action of psychotropic drugs is discussed. Attempts have been made to correlate the anxiolytic activity of various drugs with their ability to inhibit cyclic AMP phosphodiesterase in brain, but the drug concentrations required for phosphodiesterase inhibition are frequently higher than those reached during therapy. A correlation between the antagonism of dopamine sensitive adenylate cyclase and the therapeutic potency of neuroleptic drugs has been established, but this does not apply to all classes of antipsychotics. The blockade of histamine sensitive adenylate cyclase appears to contribute to the antidepressive activity of certain of drugs, but no significant correlation between antihistaminic potency and clinical antidepressant action has been found. 44 references.

**003699** Shakir, Raad A.; Nanda, Rabindra N.; Lambie, David G.; Johnson, Ralph H. University Dept. of Neurology, Institute of Neurological Sciences, Southern General Hospital, Glasgow G51 4TF, Scotland **Comparative trial of valproate sodium and clonazepam in chronic epilepsy.** Archives of Neurology. 36(5):301-304, 1979.

A crossover comparative study of valproate sodium and clonazepam in the treatment of 32 adult epileptic patients receiving multiple drug therapy is described. Serum concentrations of other anticonvulsant drugs were unchanged by the addition of clonazepam. However, patients receiving high doses of other anticonvulsant drugs had lower serum concentrations of clonazepam. With valproate sodium, phenobarbital concentrations increased in patients receiving phenobarbital but not significantly in patients receiving primidone. Phenytoin concentrations were reduced during treatment with valproate sodium. Both drugs significantly reduced the frequency of minor seizures, with valproate sodium having the greater effect. However, it is important to monitor serum concentrations of other anticonvulsant drugs during treatment with valproate sodium since changes in these may influence seizure control or cause side-effects. 10 references. (Author abstract)

**003700** Szentistvanyi, Istvan; Janka, Zoltan. Lithium Research Branch, Dept. of Neurology and Psychiatry, University Medical School, P.O. Box 397, H-6701 Szeged, Hungary **Sodium-dependent lithium efflux from red cells in affective disorders.** Psychiatry Research. 1(3):265-272, 1979.

Steady state red blood cell/plasma lithium concentration ratios were determined simultaneously with the in vitro sodium dependent downhill lithium efflux from red cells during maintenance lithium treatment in 22 bipolar depressed patients, 17 unipolar depressed patients, and 28 psychiatric control patients. The values of the sodium dependent lithium efflux were significantly correlated with the steady-state lithium levels in red blood cells and plasma. A profound difference in sodium dependent lithium efflux from red cells was found between controls and bipolar patients and to a lesser degree between con-

trols and unipolar patients. 38 references. (Author abstract modified)

**003701** Tecce, Joseph J.; Cole, Jonathan O.; Mayer, Joseph; Lewis, David C. Laboratory of Neuropsychology, Boston State Hospital, 591 Morton Street, Boston, MA 02124 **Methadone effects on brain functioning and Type A and B CNV shapes.** Psychopharmacology. 65(1):21-25, 1979.

Twelve male outpatients participating in a methadone maintenance treatment program were evaluated for the effects of acute administration of methadone on brain functioning, attention performance, and psychophysiological activity. Individual differences in response to methadone were assessed by classifying patients into two groups on the basis of basal contingent negative variation shapes: type A (quick rise time) and type B (slow rise time). Methadone produced a pattern of increased electrical brain activity and enhanced attention performance in type B patients and elevated heartrate and lowered eye blink rate in type A subjects. Results are interpreted in terms of the distraction/arousal and the eye blink/hedonia hypotheses. 16 references. (Author abstract modified)

**003702** Tsang, D.; Lal, S.; Finlayson, M. H. Dept. of Biochemistry, Chinese University of Hong Kong, Shatin, NT, Hong Kong **Effect of TRH on cyclic AMP formation in human pineal gland homogenates.** Brain Research. 188(1):278-281, 1980.

The effects of hypothalamic hormones on the cyclic AMP generating system were studied in homogenates of human pineal gland. Noradrenaline (NA) stimulated the formation of cyclic AMP, and this effect was blocked by propranolol, a selective beta-adrenergic blocker. Thyrotropin releasing hormone (TRH), luteinizing hormone releasing hormone (LRH), and somatotropin release inhibiting factor (SRIF) had no effect on basal cyclic AMP formation. NA stimulated cyclic AMP formation was inhibited by TRH, but not by LRH or SRIF. Results suggest that TRH may regulate beta-adrenergic activity in the pineal gland and may also be involved in melatonin synthesis. 13 references.

**003703** Willer, J. C.; Boureau, F.; Dauthier, C.; Bonora, M. Lab. Physiol., Fac. Med. Saint-Antoine, 27, rue Chaligny, F-75571 Paris Cedex 12, France **Study of naloxone in normal awake man: effects on heart rate and respiration.** Neuropharmacology. 18(5):469-472, 1979.

The effects of naloxone and placebo on heartrate and ventilatory response were compared in six healthy volunteers. Neither naloxone nor placebo produced significant changes in the parameters studied, and there was no significant difference in results obtained with naloxone and placebo. Results are discussed in relation to the regulation of endogenous opioid systems in normal and pathological conditions. 18 references. (Author abstract modified)

## 14 MECHANISM OF ACTION: BEHAVIORAL

**003704** Belgrave, B. E.; Bird, K. D.; Chesher, G. B.; Jackson, D. M.; Lubbe, K. E.; Starmer, G. A.; Teo, R. K. C. Jackson: Dept. of Pharmacology, University of Sydney, NSW 2006, Australia New South Wales 2033, Australia **The effect of (-) trans-delta9-tetrahydrocannabinol, alone and in combination with ethanol, on human performance.** Psychopharmacology. 62(1):53-60, 1979.

The effects of a 320mg/kg dose of (-) trans-delta9-tetrahydrocannabinol alone and in combination with 0.54g/kg on the cognitive, perceptual and motor performance of 25 Ss were investigated. The measurements were made at 100, 160, 220, and 280 min after ingestion. Both THC and ethanol produced significant decrements in the general performance factor. Ethanol affected steadiness and psychomotor coordination while THC affected all four rotated factors. Peak ethanol effects wore off by the last measurement time, while performance decrements induced by THC were slower in onset and lasted longer. No interaction between the two drugs was noted, and the effect of combined doses was no more than additive. 14 references. (Author abstract modified)

**003705** Belleville, Jon P.; Dorey, Fred; Bellville, J. Weldon. Bellville, J. W.: Dept. of Anesthesiology, UCLA School of Medicine, Los Angeles, CA 90024 **Effects of nefopam on visual tracking.** Clinical Pharmacology and Therapeutics. 26(4):457-463, 1979.

Performance on a visual tracking task was used to study the hand/eye coordination of healthy male sleep deprived Ss treated with nefopam, d-amphetamine, pentazocine, or placebo. D-amphetamine (10mg orally) significantly improved tracking performance; Ss felt more able to perform the tasks, as well as more anxious, alert, steady, sociable, and strong. Pentazocine (45mg intramuscularly) caused deterioration in tracking performance, accompanied by reports of depression, gloominess, dreaminess, nausea, and injection site pain. No significant change in tracking performance or subjective effects was seen after nefopam (15 or 30mg intramuscularly) or placebo. 23 references. (Author abstract modified)

**003706** Bente, D. Klinikum Charlottenburg, Abt. fur Psychophysiologie, Nussbaumallee 34, D-1000 Berlin 19, Germany **Vigilance and evaluation of psychotropic drug effects on EEG.** Pharmakopsychiatrie Neuro-Psychopharmakologie. 12(2):137-147, 1979.

Vigilance and evaluation of psychotropic drug effects on EEG are discussed and illustrated using data from a study of viloxazine, a new antidepressant drug in a paper presented to the 1978 symposium Switzerland. Methodological requirements for an adequate evaluation of psychotropic drug effects on vigilance, and appropriate measurement procedures are considered. Methodological procedures are illustrated in a series of studies designed to evaluate viloxazine on waking activity under definite conditions of vigilance in the performance of pursuit tracking tasks and during driving on a special test course. Findings from these studies indicate that quantitative studies in normal subjects can reveal important aspects of neurotropic drug action and their relevance to therapeutic effect in psychiatric patients. 21 references. (Author abstract modified)

**003707** Bohus, Bela. Rudolf Magnus Institute for Pharmacology, Medical Faculty, Vondellaan 6, 3521 GD Utrecht, The Netherlands **Effects of ACTH-like neuropeptides on animal behavior and man.** Pharmacology. 18(3):113-122, 1979.

The behavioral effects of neuropeptides related to adrenocorticotopic hormone are reviewed, and their mechanism of action is discussed. These peptides have shown psychoactive effects in both human and animal studies, including effects on motivation, attention, learning, and memory. These peptides may have a role in the etiology and treatment of mental illness. 91 references. (Author abstract modified)

**003708** Burns, Marcelline; Moskowitz, H. Southern California Research Institute, 6305 Arizona Place, Los Angeles, CA 90045 **Effects of diphenhydramine and alcohol on skills performance.** European Journal of Clinical Pharmacology. 17(4):259-266, 1980.

The effects of combined ingestion of alcohol and the commonly used antihistamine, diphenhydramine on an objective behavior measure considered to be of importance for driving and other man/machine interaction situations were assessed. Behav-

ioral variables studied included a compensatory tracking task, a critical compensatory tracking task, a divided attention task consisting of the simultaneous performance of a tracking task with a visual search task, and a test of information processing rate. Data from 12 male Ss indicate performance impairment by diphenhydramine, with an additive effect under the combined drug/alcohol treatment. 10 references. (Author abstract modified)

**003709** Elliott, Henry W.; Gottschalk, Louis A.; Uliana, Reginia L. Dept. of Medical Pharmacology and Therapeutics, College of Medicine, University of California, Irvine, CA 92664 **Relationship of plasma meperidine levels ot changes in anxiety and hostility.** In: Gottschalk, L., The content analysis of verbal behavior. New York, SP Medical & Scientific Books, 1979. 977 p. (p. 449-454).

The effects of single 100mg doses of meperidine HCl, given intramuscularly and orally, on anxiety and hostility levels and on plasma concentrations of meperidine base in adult male former narcotic users were studies. Anxiety and hostility were measured by speech content analysis before and after drug administration and correlated with plasma concentrations of meperidine. Significant decreases in anxiety and outward overt hostility scores occured 1 to 1.5 hours postdrug when plasma meperidine concentrations were high, with return of these affect scores toward predrug values at 6 hours when plasma concentrations of meperidine were falling. Meperidine was found to resemble sedative hypnotics in its effects on anxiety and hostility. The findings are consistent with the hypothesis that narcotic abuse is enhanced through the psychological effects of these drugs. 17 references. (Author abstract modified)

**003710** Erdmann, Gisela; van Lindern, Beatrix. Department of Psychology, University of Dusseldorf, Uiversitatsstr. 1, D-4000 Dusseldorf, Germany **The effects of beta-adrenergic stimulation and beta-adrenergic blockade on emotional reactions** Psychophysiology. 17(4):332-338. 1980.

The effects of beta-adrenergic arousal on emotional reactions were studied. Ss received either 40mg of the beta-adrenergic blocking agent oxpreolol, placebo, or 20mg of the beta stimulating agent orciprenaline. They were placed in one of two situations designed to induce either angerlike or no emotional reactions. The drug as well as the anger situation influenced bodily changes. Under oxprenolol the anger situation had no effects on reported emotions, whereas under orciprenaline the anger situation led to an increase in reports of anxiety. 26 references. (Author abstract modified)

**003711** Fahn, Stanley; Cote, Lucien J.; Snider, Stuart R.; Barrett, Robert E.; Isgreen, William P. Neurological Institute, 710 West 168th Street, New York, NY **The role of bromocriptine in the treatment of parkinsonism.** Neurology. 29(8):1077-1083, 1979.

Fifty-three patients with parkinsonism, either with intractable symptoms despite optimum dosage levodopa therapy or with adverse effects from levodopa limiting its usefulness, were treated with bromocriptine, with gradually increasing doses until benefit or adverse effect was encountered. All were initially maintained on optimal levodopa therapy. Improvement was seen in 26 patients, of whom 19 (36% of the total 53 patients) had sustained improvement. Effective doses of bromocriptine ranged from 5 to 90mg per day. Improvement occurred in all categories of clinical problems, including patients who lost some benefit from chronic levodopa therapy as well as those with adverse effects from levodopa. A high incidence (70%) of adverse effects of bromocriptine limited the usefulness of this drug. Since one cannot predict which patients might benefit from bromocriptine, this drug is recommended in patients not doing well on levodopa therapy and if other means to improve their condition are not successful. 25 references. (Author abstract)

**003712** File, Sandra E.; Bond, Alyson J. Dept. of Pharmacology, School of Pharmacy, University of London, Brunswick Square, London WC1N 1AX, England **Impaired performance and sedation after a single dose of lorazepam.** Psychopharmacology. 66(3):309-313, 1979.

In a double-blind crossover study using normal student volunteers, the effects of 1mg and 2.5mg lorazepam on self-rated mood and bodily symptoms, as well as performance in number of tests were assessed. Both doses significantly increased self-ratings of physical and mental sedation, the effects being more marked 4 hours after drug administration than after 1 hour. Lorazepam impaired simple reaction time, verbal learning, number cancellation, symbol copying, and performance in the digit symbol substitution test. Impairments are reported to be greater with the 2.5mg dose and more marked 4 hours after drug administration than after 1 hour. 14 references. (Author abstract)

**003713** Freedman, Robert; Bell, Jon; Kirch, Darrell. University of Colorado School of Medicine, 4200 East Ninth Avenue, Denver, CO 80262 **Clonidine therapy for coexisting psychosis and tardive dyskinesia.** American Journal of Psychiatry. 137(5):629-630, 1980.

Two cases are reported in which the patient received clonidine therapy in an attempt to provide antipsychotic medication that has no antidopaminergic action to treat coexisting psychosis and tardive dyskinesia. In both cases the patients' psychotic symptoms were diminished and there was improvement in the tardive dyskinesia. Also in both cases there was a significant drop in blood pressure. While the effect on blood pressure is cause for concern, it is concluded that clonidine may be a better choice than either neuroleptics or no drug therapy for patients with tardive dyskinesia. 9 references.

**003714** Gillman, Mark A.; Kok, Lyndley; Lichtigfeld, Frederick J. 1032 Medical City, 106 Eloff Street, Johannesburg, South Africa **Paradoxical effect of naloxone on nitrous oxide analgesia in man.** European Journal of Pharmacology. 61(2):175-177, 1980.

The effects of naloxone on nitrous oxide analgesia were examined in 15 healthy volunteers. Nitrous oxide raised the pain threshhold in all Ss. Naloxone markedly lowered the nitrous oxide pain threshhold in 4 Ss, but enhanced the analgesic action of nitrous oxide in the remaining 11 Ss. Results support animal studies implicating opiate receptors in the mediation of nitrous oxide analgesia and suggest a dual system may operate in pain perception in humans. 10 references. (Author abstract modified)

**003715** Gottschalk, Louis A.; Bates, Daniel E.; Waskow, Irene E.; Katz, Martin M.; Olsson, James. Dept. of Psychiatry and Human Behavior, College of Medicine, University of California, Irvine, CA 92664 **Effect of amphetamine or chlorpromazine on Achievement Strivings scores derived from content analysis of speech.** In: Gottschalk, L., The content analysis of verbal behavior. New York, SP Medical & Scientific Books, 1979. 977p. (p. 263-269).

The effects of amphetamine and chlorpromazine on achievement strivings as measured by a content analysis method applied to speech samples are reported. A relationship was found between ingestion of 15mg of amphetamine and a significant increase in achievement Strivings scores 2 hours later. Results corroborate with other studies that single doses of psychomotor stimulants increase the expression of achievement strivings, as assessed by the Gottschalk content analysis procedures. It is concluded that the psychopharmacological validation of the Gottschalk-Gleser Achievement Strivings Scale justifies further

use of this objective content analysis procedure for assessing the magnitude of achievement strivings as a predictor variable or dependent variable in psychiatric and behavioral science research. 15 references.

**003716** Greenblatt, David J.; Shader, Richard I.; Harmatz, Jerold S.; Georgotas, Anastasios. Clinical Pharmacology Unit, Massachusetts General Hospital, Boston, MA **Self-rated sedation and plasma concentrations of desmethyldiazepam following single doses of clorazepate.** Psychopharmacology. 66(3):289-290, 1979.

Plasma concentrations of desmethyldiazepam (DMDZ) and intensity of self-rated sedation were measured at multiple during a 6 hour period after a single 15mg oral dose of clorazepate dipotassium. Mean plasma DMDZ levels and mean sedation scores both became maximal at 1.0 to 2.5 hours after drug dosage, By 6 hours, however, mean sedation had returned to the predrug baseline score while mean DMDZ concentration fell only slightly from the maximum value. Disappearance of sedation despite persistence of high DMDZ levels might be due to adaptation or tolerance, it is suggested, and, therefore, subjective effects of benzodiazepines may depend upon duration of drug exposure as well as dose and concentration. 14 references. (Author abstract)

**003717** Herning, Ronald I.; Jones, Reese T.; Peltzman, Deborah J. Langley Porter Neuropsychiatric Institute, University of California, San Francisco, CA 94143 **Changes in human event related potentials with prolonged delta9-tetrahydrocannabinol (THC) use.** Electroencephalography and Clinical Neurophysiology. 47(5):556-570, 1979.

The effect of prolonged exposure to delta9-tetrahydrocannabinol (THC) on human event related auditory evoked potentials was investigated. Auditory event related potentials and contingent negative variation from a series of behavioral tasks were recorded from 27 hospitalized volunteers before, during, and after 14 days of chronic THC intoxication at two different dosage levels. A control group consisted of 12 hospitalized volunteers. Changes in auditory evoked potentials and contingent negative variation were related to dose level and task difficulty. The amplitude of the N1 component of the auditory evoked potential was depressed at the higher dose level during the early period of THC administration. At a later testing, the N1 continued to be depressed only on the more difficult tasks. The contingent negative variation was depressed for both doses at the earlier testing and depressed only for the higher dose the most difficult task at the later testing. 21 references. (Author abstract modified)

**003718** Hindmarch, I.; Parrott, A. C.; Lanza, M. Dept. of Psychology, University of Leeds, Leeds LS2 9JT, England **The effects of an ergot alkaloid derivative (Hydergine) on aspects of psychomotor performance, arousal, and cognitive processing ability.** Journal of Clinical Pharmacology. 19(11 and 12):726-732, 1979.

The effects of an ergot alkaloid derivative (Hydergine) on several aspects of psychomotor performance, arousal, and cognitive processing ability were investigated in 10 volunteers. Effects of Hydergine, 12mg per day for 2 weeks, on mental and cognitive performance add support to biochemical findings that implicate the ergot alkaloids in cellular activity likely to increase cortical arousal and awareness. The high dose of Hydergine used in this study was exceptionally well tolerated and produced significant results on individual measures of central nervous system activity which suggest the use of similar doses in patient populations. It appears that the 2 week schedule of repeated doses is the minimum required to produce an effect on CNS activity, but even with such a dose regimen, it appears that the drug continues to exert some effect after its withdrawal. 17 references.

**003719** Hrbek, Jan; Macakova, J.; Komenda, S.; Siroka, A. Dr. S. Allende 3, 775 15 Olomouc, Czechoslovakia **Acute effects of clorotepin (2 mg), its () enantiomer (2 mg) and (-) enantiomer (2 mg) on verbal associations.** Activitas Nervosa Superior. 21(1):43-44, 1979.

The acute effects of clorotepin and its positive and negative enantiomers on higher nervous activity were studied in 16 undergraduate Ss by means of artifical conditioned speech connections. Investigation sets consisted of two optic, two complex tactile, and two acoustic associations. Dependent measures were the number of repetitions necessary for mastering the task, number of correct responses, and frequency of responses in the first eight repetitions. Analysis of variance results indicate no significant difference between drugs and placebo. 2 references.

**003720** Kales, Anthony; Scharf, Martin B.; Soldatos, Constantin R.; Bixler, Edward O.; Bianchi, Susan B.; Schweitzer, Paula K. Sleep Research and Treatment Center, Milton S. Hershey Medical Center, Hershey, PA 17033 **Quazepam, a new benzodiazepine hypnotic: intermediate-term sleep laboratory evaluation.** Journal of Clinical Pharmacology. 20(4 Part 1):184-192, 1980.

Quazepam, a new benzodiazepine hypnotic, was evaluated in sleep laboratory studies of five insomniacs. With short-term use, sleep induction and sleep maintenance both improved; total waking time was decreased by 46%. Waking time was also significantly decreased with intermediate term use. Stage 3 sleep was unchanged with short-term administration, but significantly reduced with longer use. Stage 4 sleep was significantly decreased with short-term administration and abolished with longer use. 21 references. (Author abstract modified)

**003721** Kitahama, Kunio; Valatx, Jean-Louis. Departement de Medecine Experimentale, Universite Claude-Bernard, 8, avenue Rockefeller, F-69373 Lyon Cedex 2, France **Strain differences in amphetamine sensitivity in mice: II. Over compensation of paradoxical sleep after deprivation in two C57 strains.** Psychopharmacology. 66(3):291-295, 1979.

Genetic differences in the mode of amphetamine-induced paradoxical sleep (PS) suppression, subsequent PS rebound, and dependence of these effects on dose, strain, and time of injection were studied. Three inbred strains of mice with differing sleep/wakefulness cycles were used and long-term polygraphic recordings were carried out. Methylamphetamine induced wakefulness for 3 to 5 hours followed by PS rebound in C57BR, C57BL/6, and BALB/c mice. Slow-wave sleep and PS suppression time were proportional to the given dose and different among strains. Suppression time was also dependent on the time of injection. Later PS rebound was significant in C57 strains, and in certain cases greater than PS loss, whereas rebound was small in BALB/c mice and PS loss was not completely compensated. 32 references. (Author abstract modified)

**003722** Kohnen, Ralph; Lienert, Gustav A. Dept. of Cultural and Educational Sciences, University of Erlangen-Nurnberg, Nurnberg, Germany **Defining tranquilizers operationally by non additive effect in experimental stress situations.** Psychopharmacology. 68(3):291-294, 1980.

The effects of cloxazolam on performance on association memory tasks were studied in normal Ss under conditions of low, medium, and high social stress. Results indicated that drug improved performance under high stress conditions, but had a detrimental effect under low stress conditions. Results are discussed in relation to the nonadditivity hypothesis. 9 references. (Author abstract modified)

**003723** Muller-Oerlinghausen, B.; Hamann, S.; Herrmann, W. M.; Kropf, D. Psychiatrische Klinik der FUB, Nussbaum-Allee 36, D-1000 Berlin 19, Germany **Effects of lithium on vigilance, psychomotoric performance, and mood.** Pharmakopsychiatrie Neuro-Psychopharmakologie. 12(5):388-396, 1979.

Psychometric and neuropsychophysiological results derived from a study of normal volunteers given either lithium or placebo are presented. The subjects were tested after 1 and 2 weeks using quantitative pharmaco-EEG tests, psychological performance tests, and mood scales. In comparison to placebo, lithium shows decreased flicker fusion threshold and mood changes toward depression. In the resting EEG a decrease of relative slow alpha, an increase of relative fast beta, and increase of power were observed. The results suggest that lithium leads to decreased vigilance and reduced spontaneous activity. 53 references. (Author abstract modified)

**003724** Munjack, Dennis J. Adult Out-Patient Dept., University of Southern California Medical Center, Los Angeles, CA 90033 **Sex and drugs.** Clinical Toxicology. 15(1):75-89, 1979.

Drugs that alter erection or ejaculation, affect sexual drive or erotic interest are discussed. The neurological and endocrinological effects of alcohol are examined. Other drugs that are considered include cocaine, amphetamines, hallucinogens, and marijuana. The relationships between neurotransmitters, central amines, and sexual responses are evaluated. Drugs that apparently impair sexual response include propranolol, alpha-methyl dopa, and various central nervous system depressants. Central stimulatory effects on sexual interest may or may not outweigh any potential peripheral effects antagonistic to sexual functioning. 36 references.

**003725** Nicholson, A. N.; Stone, Barbara M. Royal Air Force Institute of Aviation Medicine, Farnborough, Hampshire, England **L-tryptophan and sleep in healthy man.** Electroencephalography and Clinical Neurophysiology. 47(5):539-545, 1979.

The effects of L-tryptophan on daytime and nighttime sleep were investigated. Subjects were six healthy male adults. A limited dose range was used in order to avoid the possibility of nonspecific effects. In comparison with placebo, no effect on nocturnal sleep was observed. With the largest daytime doses, an increases in the duration of stage 3 sleep was observed. The results provided marginal evidence that REM sleep may be modified by L-tryptophan. It is concluded that the hypnotic activity of L-tryptophan is limited and uncertain. 16 references. (Author abstract modified)

**003726** Ogura, C.; Nakazawa, K.; Majima, K.; Nakamura, K.; Ueda, H.; Umezawa, Y.; Wardell, W. M. Dept. of Neuropsychiatry, School of Medicine, Tottori University, Yonago, 683, Japan **Residual effects of hypnotics: triazolam, flurazepam, and nitrazepam.** Psychopharmacology. 68(1):61-65, 1980.

The residual effects of three hypnotics were assessed in 16 healthy volunteers, using 24 hour polygraphy. Triazolam (0.25 and 0.5mg), flurazepam (30mg), and nitrazepam (10mg) showed definite sleep inducing and sleep maintenance effects in night recordings. Flurazepam (15 and 30mg) and nitrazepam (5 and 10mg) caused residual effects in the morning, afternoon, and evening recording periods on the day after hypnotic administration. No effects were seen on the day after administration of 0.25 or 0.5mg triazolam, except some slight residual effects in the morning. 14 references. (Author abstract modified)

**003727** Persson, Lars-Olof; Sjoberg, Lennart; Svensson, Erland. Sjoberg: Dept. of Psychology, University of Goteborg, Goteborg, Sweden **Mood effects of alcohol.** Psychopharmacology. 68(3):295-299, 1980.

Mood ratings were obtained from 11 Ss during the 3 hours after administration of 0.41, 0.63, or 0.85g/kg alcohol. Ss felt euphoric and extraverted and less tense after the highest dose, but lower doses induced more negative feelings. Frequent drinkers reported greater affective benefit from alcohol than rare drinkers. 21 references. (Author abstract modified)

**003728** Rogers, Peter J.; Blundell, John E. Psychology Dept., University of Leeds, Leeds LS2 9JT, England **Effect of anorexic drugs on food intake and the micro-structure of eating in human subjects.** Psychopharmacology. 66(2):159-165, 1979.

The effects of oral doses of amphetamine or fenfluramine on food intake and the fine structure of eating were examined. Subjects were six male and six female volunteers of normal weight, aged 19 to 26. Amphetamine and fenfluramine showed generally similar effects on food intake and on the subjective experience of hunger, but displayed differing actions on the fine structure of eating. Amphetamine increased latency to initiation of eating and increased the rate of food ingestion, whilst fenfluramine slowed the local rate of eating and eliminated the characteristic decline in the rate of feeding across the course of a meal. These findings display certain resemblances to the results of animal experiments involving similar pharmacological manipulations and emphasize the importance of measuring rate of feeding in animal and human studies. Such microanalysis of feeding behavior not only provides a tool for understanding systems involved in the modulation of food consumption but also reveals information helpful in the use of drugs for treatment of obesity. 32 references. (Author abstract modified)

**003729** Rothenberg, S.; Peck, E. A.; Schottenfeld, S.; Betley, G. E.; Altman, J. L. Alcohol and Drug Abuse Research Center, McLean Hospital, Belmont, MA 02178 **Methadone depression of visual signal detection performance.** Pharmacology Biochemistry and Behavior. 11(5):521-527, 1979.

A previously reported slowing of simple visual reaction time in subjects receiving single doses of oral methadone was investigated. Three well trained subjects performed a modified double flash detection task several times after single doses of 5mg and 10mg of oral methadone and a placebo. A Theory of Signal Detectability analysis allowed for a clear distinction between drug-induced changes in visual sensitivity and changes in response bias. It was found that methadone reduced visual sensitivity. The peak depression in detection as well as the duration of the depressed performance were dose related. Depression in performance paralleled the subjective effect of the drug in each subject. Averaged visual evoked potentials showed significant changes in peak drug effect to the onset of each of the pair of stimuli. It is concluded that methadone depresses visual function by acting on the visual parts of the central nervous system. The retina, midbrain, and thalamic visual nuclei are discussed as possible sites of action of methadone. 22 references. (Author abstract)

**003730** Scharf, Martin B.; Bixler, Edward O.; Kales, Anthony; Soldatos, Constantin R. Sleep Research and Treatment Center, Milton S. Hershey Medical Center, Hershey, PA 17033 **Long-term sleep laboratory evaluation of flunitrazepam.** Pharmacology. 19(4):173-181, 1979.

The effectiveness of flunitrazepam for inducing and maintaining sleep was evaluated in six insomniac Ss given 2mg of the drug nightly for 4 consecutive weeks. Sleep laboratory evaluations showed that the drug was effective for short-term use. However, tolerance developed for sleep maintenance during the intermediate and long-term drug administration periods. Follow-

ing drug withdrawal, sleep was significantly worse than in the baseline, predrug period. Results are consistent with previous findings of rebound insomnia following withdrawal of short and intermediate actingbenzodiazepines. 23 references. (Author abstract modified)

**003731** Shute, C. C. D. no address **The McCollough effect: an indicator of central neurotransmitter activity.** New York, Cambridge University Press, 1979. 149 p. $24.50.

The utility of the McCullough effect, wherein presentation of a pattern associated with a particular color sets up changes in the brain so that subsequent presentations of the pattern cause a phantom complementary color to be seen, as an indicator of central neurotransmitter activity is explored. It is hypothesized that the McCullough effect is important in the study of memory and forgetting, and that there is a strong cholinergic aspect to it. The effects of various psychopharmacological agents on the McCullough effect are described: hyoscine enhances it strongly, as does ethopropazine, while the benzodiazepines inhibit its decay.

**003732** Szabadi, E.; Bradshaw, C.M.; Gaszner, P. Dept. of Psychiatry, University of Manchester, Stopford Bldg., Oxford Road, Manchester M13 9PT, England **The comparison of the effects of DL-308, a potential new neuroleptic agent, and thioridazine on some psychological and physiological functions in healthy volunteers.** Psychopharmacology. 68(2):125-134, 1980

The effects of 1-(3-chlorophenyl)-3-(2-(3,3-dimethyl-1-azetidinyl) ethyl)imidazolidin-2-one (DL-308) were compared with those of thioridazine in healthy male volunteers. DL-308 displayed more potent sedative properties than thioridazine and had a faster time course of action. Both drugs caused miosis, hypotension, and decreased salivation. When equisedative doses of the two drugs were given, DL-308 had a much smaller influence on automatic functions than thioridazine. Neither drug significantly affected the motor system. DL-308 increased subjectively rated sweating and objectively measured heartrate. 21 references. (Author abstract modified)

**003733** Weiss, Kenneth J.; Ciraulo, Domenic A.; Shader, Richard I. Dept. of Psychiatry and Human Behavior, Thomas Jefferson University Hospital, 414 Main Building, Philadelphia, PA 19107 **Physostigmine test in the rabbit syndrome and tardive dyskinesia.** American Journal of Psychiatry. 137(5):627-628, 1980.

Two cases which illustrate the reciprocal relationship between tardive dyskinesia and parkinsonism or the rabbit syndrome are reported. The two patients were over 60 years old and had substantial exposure to neuroleptics and antiparkinson drugs. Physostigmine was used to differentiate tardive dyskinesia from the rabbit syndrome. It caused the rabbit movements to be accentuated and the athetoid dyskinetic movements to recede. It is suggested that the rabbit syndrome may be the result of a chronic cholinergic blockade that gives rise to a denervation type supersensitivity analogous to the dopaminergic supersensitivity of tardive dyskinesia. 10 references.

**003734** Zahn, Theodore P.; Rapoport, Judith L.; Thompson, Christine L. Building 31, Room 4C39, NIMH, Bethesda, MD 20205 **Autonomic and behavioral effects of dextroamphetamine and placebo in normal and hyperactive prepubertal boys.** Journal of Abnormal Child Psychology. 8(2):145-160, 1980.

The hypothesis that the response to dextroamphetamine in terms of activity, attention, impulsivity, and autonomic activity is similar in normal (N), and hyperactive (H) children was tested on three occasions: off drug (day 1) and after ingestion (double-blind) of placebo and of .5 mg/kg dextroamphetamine. Both N and H groups showed drug effects of reduced motor activity and impulsivity, improved attention (reaction time task), increased heartrate (HR) and HR slowing during reaction time foreperiods, and decreased finger temperature. Both groups also had decreases in skin conductance responsivitiy but in different parts of the test. Placebo compared to day 1 produced increased activity and autonomic arousal, but no change in reaction time. Stimulant drugs thus have similar behavioral and autonomic effects in both N and H boys, but the beneficial effects on behavior do not depend critically on increases in arousal. 26 references. (Author abstract modified)

## 15 TOXICOLOGY AND SIDE EFFECTS

**003735** Ananth, J. 1025 Pine Ave., W., Montreal, Quebec, H3A 1A1 Canada **Tardive dyskinesia: myths and realities.** Psychosomatics. 21(5):389-391, 394-396, 1980.

Studies of tardive dyskinesia are reviewed. First signs and prognosis, varieties of dyskinesia, predisposing factors, and incidence are examined. Precipitating factors, reversibility, and the role of medication are discussed. It is reported that tardive dyskinesia is a clinically distinct syndrome with characteristic involuntary movements, most often associated with the administration of neuroleptic drugs. The syndrome is not found to be as prevalent as previously indicated. Suggestions for treatment, for use of neuroleptics, and for discussing side-effects with some patients are made. 75 references. (Author abstract modified)

**003736** Ananth, J.; Ghadirian, A. M. Dept. of Psychiatry, McGill University, Montreal, Quebec 1821, Canada **Drug-induced mood disorders.** International Pharmacopsychiatry. 15(1):59-73, 1980.

Drug-induced depressions caused by various drugs including antihypertensives, anxiolytics, antibiotics, antidepressants, corticosteroids, choline, indomethacin, levodopa, metronidazole, neuroleptics, oral contraceptives, sulphonamides, and physostigmine are considered. Clinically these drug-induced depressions may go unnoticed and thus create therapeutic problems. Although causal relationships are difficult to establish, depression occurring during the course of drug treatment needs an evaluation of all the medications that the patient has been receiving. Postpsychotic depressions are divided into three types of depression: pendular depression, primarily disease related; chronic depression, primarily environment related; and amine depletion depression, drug related. Thus, drug-induced depressions are viewed as constituting a subgroup of postpsychotic depression. It is argued that it is essential to carefully monitor patients receiving drugs known to produce depression, because prompt recognition of the drug-induced depressions may assist in initiating proper therapeutic measures. 125 references. (Author abstract modified)

**003737** Annitto, William J.; Layman, William A. Dept. of Psychiatry, 65 Bergen Street, Martland Hospital Unit, 10th Floor, Newark, NJ 07103 **Anabolic steroids and acute schizophrenic episode.** Journal of Clinical Psychiatry. 41(4):143-144, 1980.

A case is described which temporally relates the use of anabolic steroids with the development of an acute schizophreniform illness. Although the use of anabolic steroids by athletes to increase physical performance has vastly increased over the last 10 years, there is almost no clinical literature on this particular side-effect. Diagnostic implications of the use of anabolic steroids are considered, and it is recommended that psychiatrists consider this side-effect in the differential diagnosis of schizophrenic episodes. The notion of a whole subculture of abusers of substances with potential for producing schizophreniform disorders is discussed. 5 references. (Author abstract modified)

**003738** Asnis, Gregory M.; Sachar, Edward J.; Langer, Gerhard; Halpern, Frieda S.; Fink, Max. New York State Psychiatric Institute, 722 West 168th St., New York, NY 10032 **Normal prolactin responses in tardive dyskinesia.** Psychopharmacology. 66(3):247-250, 1979.

Whether dopamine hypersensitivity extends to the tuberoinfundibular dopamine (TIDA) system, which regulates by inhibition, pituitary prolactin secretion was assessed in six patients with tardive dyskinesia. Plasma prolactin concentrations were studied during chronic haloperidol therapy; serially after abrupt halpoperidol withdrawal; while unmediated; and in response to an acute dose of 0.5mg i.m. haloperidol. In all four conditions, prolactin responses did not differ from those observed in normal subjects and schizophrenics without tardive dyskinesia. It is concluded that there is no evidence for postsynaptic dopamine hypersensitivity in the TIDA pituitary pathway in patients with tardive dyskinesia. It is futher suggested that neuroleptic-induced dopamine hypersensitivity does not occur in the TIDA pituitary pathway in patients with tardive dyskinesia. It is further suggested that neuroleptic-induced dopamine hypersensitivity does not occur in the TIDA pituitary system in humans, since it was not manifest in these tardive dyskinesia patients who would be thought particularly prone to develop it. 21 references. (Author abstract modified)

**003739** Baldessarini, Ross J. Mailman Laboratories for Psychiatric Research, McLean Division of Massachusetts General Hospital, Belmont, MA 02178 **The pathophysiological basis of tardive dyskinesia.** Trends in NeuroSciences. 2(5):133-135, 1979.

Possible mechanism involved in the pathogenesis of tardive dyskinesia, a disease characterized by involuntary movements and thought to be associated with proloned clinical exposure to neuroleptic/antipsychotic drugs, are discussed. There is strong evidence that dopamine receptor supersensitivity may be involved, although not all of the evidence available is compatible with this suggestion. Indications for improved medication for the mental disorders treated with neuroleptics are resulting from work in the field. 6 references.

**003740** Bech, P.; Thomsen, J.; Prytz, S.; Vendsborg, P. B.; Zilstorff, K.; Rafaelsen, O. J. Psychochemistry Institute, Rigshospitalet, 9, Blegdamsvej, DK-2100 Copenhagen O, Denmark **The profile and severity of lithium-induced side effects in mentally healthy subjects.** Neuropsychobiology. 5(3):160-166, 1979.

The side-effects of therapeutic serum lithium levels (0.7 to 1.1mmol/1) were studied for 6 months in 26 nonpsychiatric patients via a double-blind, placebo controlled crossover design. The side-effects were measured by self-rating scales and independent observer rating scales administered every 2 to 4 weeks throughout the study. After months of treatment, lithium-induced hand tremor and thirst/polyuria were noted. These effects were not related to serum levels of lithium. The frequency of tremor was highest in patients above the age of 60 years. No initial sedative-like lithium effect was found. 22 references. (Author abstract modified)

**003741** Bernstein, Richard A. Medical Alumni Building, Burlington, VT 05401 **Malignant neuroleptic syndrome: an atypical case.** Psychosomatics. 20(12):840, 845-846, 1979.

A case report detailing the course of a patient with recurrent hyperthermia is presented and discussed. The case represents the so called malignant neuroleptic syndrome, a serious idiosyncratic reaction that occurs without respect to the ambient temperature. Included in the discussion are some clinical guidelines for the recognition of the syndrome, a review of the suspected pathophysiology, and a consideration of other hyperthermias with which the syndrome might be confused. 14 references.

**003742** Bertolini, R. Servizi Psichiatrici di Zona, Turin, Italy / **Accidents with psychotropic drugs in the aged: a personal series./** Incidenti dei farmaci psicotropi nell'anziano: casistica personale. Minerva Psichiatrica. 20(4):237-244, 1979.

The increasing likelihood of accidents with psychotropic drugs in elderly patients is discussed. It is contended that the pharmacokinetics of medicines in the aged must be understood; that the exact state of the main functions involved in such pharmakinetics must be determined in each case; that drugs must be given at the lowest possible dosage; and that treatment must not be continued any longer than necessary. An account is given of a series of 30 hospitalized aged patients and their accidents due to the side-effects of psychotropic drug usage. 15 references. (Journal abstract modified)

**003743** Bonnyns, M.; Glinoer, D.; Ermans, A. M. Service de Medecine Interne, Hopital Saint-Pierre, Universite Libre de Bruxelles, Rue Haute 322, B-1000 Brussels, Belgium /**Secondary effects of lithium on thyroid function: mechanisms, diagnosis and treatment./** Effets secondaires du lithium sur la fonction thyroidienne: mecanismes, diagnostic et traitement. Acta Psychiatrica Belgica. 79(5):570-577, 1979.

The literature concerning the side-effects of lithium on thyroid function was reviewed. Two kinds of side-effects are reported. The first type is minor, temporary, without important modification of thyroid function, and need not be treated. The second type is major and followed by hypothyroidism. This situation is usually associated with the preexistence of an autoimmune thyroiditis or another thyroid abnormality. The mechanisms responsible for lithium side-effects are described, and different thyroid examinations that should be conducted before and during lithium therapy are suggested. The indications of thyroxine administration are noted. 15 references. (Journal abstract modified)

**003744** Bowers, Malcolm B., Jr.; Study, Robert E. Dept. of Psychiatry, Yale University School of Medicine, New Haven, CT 06510 **Cerebrospinal fluid cyclic AMP and acid monoamine metabolites following probenecid: studies in psychiatric patients.** Psychopharmacology. 62(1):17-22, 1979.

The effect of probenecid treatment on cyclic cAMP levels in the lumbar cerebrospinal fluid (CSF) of psychiatric patients was studied. At levels greater than 10micro CSF cAMP was independent of CSF probenecid concentration. At these levels, cAMP transport out of CSF is probably maximally blocked and cAMP levels reflect cAMP release into CSF. CSF cAMP was significantly higher in research diagnostic criteria diagnosed schizophrenics than in other psychotics or in depressives. A significant decrease in CSF cAMP was found in psychotic patients treated with cloropromazine. No changes in CSF cAMP were observed in patients treated with tricyclic antidepressants or lithium. 39 references. (Author abstract)

**003745** Clark, Elisabeth O.; Glanzer, Murray; Turndorf, Herman. Glanzer: Dept. of Psychology, New York University, 6 Washington Pl., Room 550, New York, NY 10003 **The pattern of memory loss resulting from intravenously administered diazepam.** Archives of Neurology. 36(5):296-300, 1979.

A word recognition task was designed to determine the stage in memory affected by a single 10mg intravenous injection of diazepam and the duration of the effect. Injection in three experimental Ss produced an anterograde amnesia for the 14 to 24 minute period immediately after injection. Memory loss resulted from impaired storage, the stage during which information is entered into memory. Retention and retrieval stages of memory were unaffected. This temporary amnesia may result from increased inhibition in the hippocampal system produced by diaze-

pam, which shares many properties with the inhibitory neurotransmitter gamma-aminobutyric acid. 35 references. (Author abstract)

**003746** Coffey, C. Edward; Ross, Donald R. Dept. of Psychiatry, Duke University Medical Center, Box 3233, Durham, NC 27710 **Treatment of lithium/neuroleptic neurotoxicity during lithium maintenance.** American Journal of Psychiatry. 137(6):736-737, 1980.

A case history is described of a female manic patient who experienced a neurotoxic reaction after combined lithium/neuroleptic treatment. The toxic effects caused extrapyramidal symptoms (tremor, cogwheel, rigidity), motor slowing, and mental status changes (drowsiness and intermittent confusion). She was successfully treated by discontinuing the neuroleptic (chlorpromazine and haloperidol) and reducing the lithium to a maintenance dose. 9 references.

**003747** Cutler, Neal R.; Heiser, John F. NIMH, Bldg. 10, Rm. 3S239, 9000 Rockville Pike, Bethesda, MD 20205 **Leukopenia following treatment with thiothixene and haloperidol.** Journal of the American Medical Association. 242(26):2872-2873, 1979.

A case of leukopenia that developed in a patient on two separate occasions following treatment with thiothixene and haloperidol, respectively, is reported. The patient's leukocyte count rose to normal within a few days after administration of each antipsychotic agent was discontinued. Throughout 6 months of subsequent treatment with a phenothiazine, fluphenazine hydrochloride, the patient's hematologic count remained within normal limits. It is concluded that, although both immunologic and toxic mechanisms for the drug-induced leukopenias have been implicated, neither could be established due to the unavailability of both bone marrow and antibody studies. 3 references.

**003748** de Groot, M. H. L. 470 Peel Street, Tamworth, New South Wales, Australia **Chlormethiazole dependency -- a case report.** Australian and New Zealand Journal of Psychiatry. 13(4):349-351, 1979.

A case of dependency on chlormethiazole edisylate, a hypnotic drug with a marked anticonvulsant property, is reported in a 40-year-old woman with a previous history of other dependencies (benzodiazepines and alcohol). The patient had a background history of paternal alcoholism and reported epilepsy in a brother. At time of admission it was estimated that the patient was taking between 100 and 200 capsules a week. On admission, the patient was allowed 12 capsules per day with a daily reduction of two capsules. By the third day, the patient appeared confused and rambling in her speech; visual hallucinations and the possibility of a seizure were suspected. During confused periods, she also exhibited episodes of aggression and inappropriate laughter. Restlessness and muscular twitching were also observed. By day 11 of hospitalization, chlormethiazole had been phased out, and it was possible to reduce phenytoin and chlorpromazine. Discharge occured on day 18 of hospitalization. The possibility of suicide and the potential for dependency with chlormethiazole are discussed. 5 references. (Author abstract modified)

**003749** De Vanna, M.; Lorenzi, E.; Verrienti, P. Clinica Psichiatrica, Universita Trieste, Trieste, Italy **/EEG abnormalities during treatment with psychotropic drugs./** Anomalie elettroencefalografiche durante il trattamento con psicofarmaci. Minerva Psichiatrica. 20(4):227-236, 1979.

Correlations between EEG abnormalities induced by psychotropic drugs, and the EEGs of patients not submitted to such treatment were examined. Previously promising compounds such as imipramine have disappointed expectations, while others that were considered severe cerebral activators of paroxysmal conditions have proved less incisive than was previously thought. Quadricyclic (maprotiline), lithium salts, and new neuroleptics (clozapine) not only trigger more abnormal pictures but are also responsible for convulsive attacks at therapeutic doses. Possible clinical bioelectric correlations are hypothesized, and it is suggested that they be considered when implementing psychotropic drug treatment. 36 references. (Journal abstract modified)

**003750** de Zeeuw, R. A.; Westenberg, H. G. M.; Van Der Kleijn, E.; Gimbrere, J. S. F. Department of Toxicology, State University, Deusinglaan 2, 9713 AW Groningen, The Netherlands **An unusual case of carbamazepine poisoning with a near-fatal relapse after two days.** Clinical Toxicology. 14(3):263-269, 1979.

A case of carbamazepine poisoning is reported. A 23-year-old epileptic female took an overdose of a drug containing carbamazepine, an anticonvulsant, in an apparent suicide attempt. Plasma levels of the drug were monitored using high performance liquid chromatography. After emergency gastric aspiration procedures and 2 days of plasma monitoring, a dramatic rise in plasma concentration of carbamazepine and its metabolite occurred and the patient relapsed into a deep coma. After further treatment with a laxative of activated charcoal and sodium sulfate, the patient recovered within 4 days. The possible mechanisms underlying these occurrences and potential treatment measures are discussed. 13 references. (Author abstract modified)

**003751** Direnfeld, Lorne K.; Feldman, Robert G.; Alexander, Michael P.; Kelly-Hayes, Margaret. Feldman: Boston University Medical Center, 80 East Concord St., Boston, MA 02118 **Is L-DOPA drug holiday useful?** Neurology. 30(7, part 1):785-788, 1980.

In nine patients on long-term L-DOPA therapy for severe, chronic Parkinson disease, akinesia and other dopaminergic side-effects were ameliorated by a 3 to 21 day suspension of drug treatment. After reinstitution of L-DOPA therapy, often at lower doses than those used previously, parkinsonian signs improved. Complications of immobility were seen in two patients; one had deep vein thrombophlegitis and the other became depressed. Results suggest that a holiday from L-DOPA therapy may extend the drug's usefulness in treating Parkinson disease, possibly by resensitizing striatal dopamine receptors. 8 references. (Author abstract modified)

**003752** Fahmy, Nabil R.; Malek, Nabil S.; Lappas, Demetrios G. Dept. of Anesthesia, Massachusetts General Hospital, Boston, MA 02114 **Diazepam prevents some adverse effects of succinylcholine.** Clinical Pharmacology and Therapeutics. 26(3):395-398, 1979.

The effects of pretreatment with diazepam (0.05mg/kg i.v.) or d-tubocurarine (0.05mg/kg) were compared in patients anesthetized with succinylcholine (SCh, 1mg.kg i.v.). The muscle fasciculations, elevated serum potassium and creatinine phosphokinase levels, increased heartrate and arterial pressure, and postoperative myalgia associated with SCh administration were prevented by diazepam pretreatement. The neuromuscular blocking action of SCh was not affected by diazepam. Pretreatment with d-tubocurarine decreased the onset and magnitude of SCh-induced muscle paralysis, increased the incidence of postoperative myalgia, and did not abolish the increase in serum potassium and creatinine phosphokinase levels. Results indicate that diazepam is more effective than d-tubocurarine in preventing the adverse effects of SCh. 14 references. (Author abstract modified)



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**003753** Fontana, A.; Grob, P. J. Section of Clinical Immunology, Dept. of Medicine, University Hospital, Ramistr. 100, CH-8091 Zurich, Switzerland **Immunodeficiency in epilepsy: a new view.** Journal of Neurology. 220(4):297-301, 1980.

A followup study of epileptic patients with subnormal IgA serum concentrations indicated that IgA deficiency is a stable rather than transitory phenomenon. The most pronounced changes in IgA levels were seen in patients whose hydantoin medication had been altered. However, IgA levels remained low in some patients even after hydantoin medication was withdrawn. 10 references. (Author abstract modified)

**003754** Glen, A. I. M.; Dodd, M.; Hulme, E. B.; Kreitman, N. MRC Brain Metabolism Unit, Thomas Clouston Clinic, 153 Morningside Drive, Edinburgh, Scotland **Mortality on lithium.** Neuropsychobiology. 5(3):167-173, 1979.

A mortality study of lithium which is based on a register of patients receiving lithium since 1967 in the Edinburgh and Lothian area of Scotland is described. Information was obtained on 784 patients receiving lithium for a period of up to 115 months (97.4% of the population available for study). Thirty-three patients died during the period of study due predominantly to cardiovascular causes or to suicide. There is nothing to suggest that long-term exposure caused more deaths than short-term exposure and the pattern of mortality resembles that found in other studies of manic-depressive illness, i.e., the majority of deaths occur in the early stages of followup. 14 references. (Author abstract modified)

**003755** Gomez, Joan; Scott, Geoffrey. Westminster Hospital, London SW1, England **Hypothyroidism, psychotropic drugs and cardiotoxicity.** British Journal of Psychiatry. 136(Jan):89-91, 1980.

A case history in which hypothyroidism presented as acute psychosis and the patient was hypersensitive to phenothiazines is presented. It is suggested that hypothyroidism should be borne in mind when acute psychosis presents with atypical features and a serum thyroxine estimation should be included in the initial screening. It is also proposed that, as there appears to be some ground for implicating phenothiazines with adverse cardiac reactions in certain patients, haloperidol should be the drug of choice in acute psychosis where there is a possibility of an organic cause. 24 references.

**003756** Greenblatt, David J.; Allen, Marcia Divoll; Harmatz, Jerold S.; Noel, Barbara J.; Shader, Richard I. Clinical Pharmacology Unit, Massachusetts General Hospital, Boston, MA 02114 **Overdosage with pentobarbital and secobarbital: assessment of factors related to outcome.** Journal of Clinical Pharmacology. 19(11 and 12):758-768, 1979.

Factors related to clinical outcome following acute overdosage with pentobarbital or secobarbital were assessed in a series of 162 patients hospitalized during the period 1962 to 1975. Serious intoxication was common, and intubation and assisted ventilation were required in 59% of patients. Twenty-three percent of patients developed clinically important hypotension. Multiple regression and discriminant function analyses, performed on a subset of 88 patients for whom complete data were available, indicate that plasma barbiturate concentration and/or ingested dose were the most important correlates of serious intoxication among identifiable variables available on admission. Coingestion of other CNS depressants, such as ethanol, had no obvious effect on outcome. 25 references. (Author abstract modified)

**003757** Haglund, Kjell; Seideman, Peter; Collste, Per; Borg, Karl-Olof; von Bahr, Christer. Seideman: Dept. of Internal Medicine, Huddinge Hospital, S-141 86 Huddinge, Sweden **Influence of pentobarbital on metoprolol plasma levels.** Clinical Pharmacology and Therapeutics. 26(3):326-329, 1979.

The effects of pentobarbital on plasma levels of metoprolol were studied in eight healthy student volunteers. The area under the plasma/time curve after 0.1gm metoprolol was reduced by a mean of 32% after treatment with 0.1gm pentobarbital at bedtime for 10 days. There was considerable interindividual variability in the reduction after pentobarbital treatment (2 to 46%). 10 references. (Author abstract modified)

**003758** Hale, Mahlon S.; Bellizzi, John. University of Connecticut Health Center, Farmington, CT 06032 **Low dose perphenazine and levodopa/carbidopa therapy in a patient with Parkinsonism and a psychotic illness.** Journal of Nervous and Mental Disease. 168(5):312-314, 1980.

An unusual case is presented of a patient with Parkinson's disease and a psychosis who was treated with levodopa/carbidopa and a very low dose of pherphenazine. The case raises the issue of whether or not patients with profound psychological reactions to antiparkinson agents may be maintained on antiparkinsonian therapy by the addition of phenothiazines. 18 references. (Author abstract modified)

**003759** Hall, Richard C. W.; Stickney, Sondra K.; Gardner, Earl R.; Perl, Mark; Pfefferbaum, Betty. Dept. of Psychiatry, University of Texas Medical School, 6400 West Cullen, Houston, TX 77030 **Steroid psychoses: forms of presentation and management.** World Journal of Psychosynthesis. 11(3):33-36, 1979.

The controversies surrounding the use of steroids and the psychiatric presentation that may follow their use are reviewed along with a report of experience with this condition and its treatment. Psychotic reactions are most likely to develop in patients receiving in excess of 40mg a day of prednisone or its equivalent, and the majority of these reactions occur within the first 5 days of therapy. It is suggested that there is nothing characteristic about the presentation of steroid psychosis except its extreme variability. Emotional lability, severe anxiety, distractability, pressured speech, sensory flooding, insomnia, depression, perplexity, agitation, mutism, and apathy are commonly seen. Phenothiazines produced excellent response in all patients to whom they were administered. It is concluded that the presence of the steroid psychosis does not herald the future development of a spontaneously occurring psychosis or affective disorder. 18 references.

**003760** Hill, Reba M.; Stern, Leo. Stern: Department of Pediatrics, Rhode Island Hospital, Providence, RI 02902 **Drugs in pregnancy: effects on the fetus and newborn.** Current Therapeutics. 20(2):131-133, 135-136, 140-142, 144-147, 150, 1979.

The effects on the fetus and newborn of drugs taken in pregnancy are discussed. A table showing the effects for different agents, classified along the lines of the major categories of the effects produced, is given. A clustering of malformations are present in infants exposed in utero to anticonvulsant drugs that now make them an identifiable group. Children exposed in utero to phenytoin or phenobarbitone should be followed closely for evidence of malignancy. There are isolated reports in the literature that the psychotropic agents classified as mood elevators are teratogenic. It is concluded that fetal effects primarily of a toxic or negative nature have become a major problem in pregnancy associated therapeutics.

**003761** Howie, J. G. R.; Bigg, A. R. Dept. of General Practice, University of Aberdeen, Foresterhill Health Centre, Aberdeen AB9 2AY, Scotland **Family trends in psychotropic and antibiotic prescribing in general practice.** British Medical Journal. 280(6217):836-838, 1980.

A 10 year retrospective study of the consultations of 50 families with a city general practice was used to test the hypothesis that mothers who receive an excess of psychotropic drugs have children who receive an excess of antibiotics for episodes of acute respiratory illness. The children of the 10 mothers classed as high psychotropic users were seen twice as often with acute respiratory illness and received twice as many antibiotics as children of mothers who had received no psychotropic medication. The association between high psychotropic use was not linked in time; and indeed, the time of highest antibiotic use coincided with when the mothers received fewest psychotropic prescriptions. It is suggested that in many of these consultations, the mother rather than the child, should have been treated. 9 references. (Author abstract)

**003762** Hyman, Nigel M.; Dennis, Paul D.; Sinclair, Keith G. A. Dept. of Neurology, Radcliffe Infirmary, Oxford, England **Tremor due to sodium valproate.** Neurology. 29(8):1177-1180, 1979.

Four patients developed postural tremor after ingestion of sodium valproate. The tremor was recorded by a variable capacitance transducer and was of the benign essential type. The dosage of sodium valproate varied between 1,000mg and 2,000mg daily and serum levels were between 34.9mcg/ml and 154.3mcg/ml. Tremor was ameliorated in two cases when the dosage was reduced. In only one case was the serum level in the toxic range. The pharmacology of essential tremor is unknown; production of a similar tremor by a drug could serve as a biochemical model. 9 references. (Author abstract)

**003763** Janowsky, David S.; Risch, Craig. Dept. of Psychiatry, University of California at San Diego, P.O. Box 109, La Jolla, CA 92037 **Amphetamine psychosis and psychotic symptoms.** Psychopharmacology. 65(1):73-77, 1979.

Fifteen previously reported cases were reviewed in which experimental injection of amphetamine psychosis occurred in nonschizophrenic drug abusers to determine whether or not Schneider's first rank symptoms actually do occur in these cases. Seven, possibly ten, cases manifested Schneider's first rank symptoms and all had World Health Organization Present State Exam symptoms which discriminated schizophrenia. This observation draws further parallels between the phenomenology of amphetamine psychosis and schizophrenic symptoms. 24 references. (Author abstract modified)

**003764** Judson, Barbara A.; Himmelberger, David U.; Goldstein, Avram. Addiction Research Foundation, 701 Welch Road, No. 325, Palo Alto, CA 94304 **The naloxone test for opiate dependence.** Clinical Pharmacology and Therapeutics. 27(4):492-501, 1980.

Naloxone tests for opiate dependence were given to 296 applicants for treatment with the surrogate opiate levomethadyl acetate and to 103 applicants for treatment with the opiate antagonist naltrexone. A dramatic decrease in withdrawal signs and symptoms elicited by naloxone was observed as Ss went from an opiate dependent to a nondependent state. A scoring guide and testing procedure based on objective signs is described. 17 references. (Author abstract modified)

**003765** Kangas, Lauri; Erkkola, R.; Kanto, J.; Eronen, M. Farmos Group Ltd., Research Center, P.O. Box 425, SF-20101 Turku 10, Finland **Transfer of free and conjugated oxazepam across the human placenta.** European Journal of Clinical Pharmacology. 17(4):301-304, 1980.

The transfer of free and conjugated oxazepam across the human placenta was investigated in 6 women 13 to 16 weeks pregnant and 12 women at 38 to 40 weeks gestation. Twelve hours prior to legal abortions (by hysterectomy in the former group and by elective caesarean section in the latter group) Ss received oral oxazepam. Concentrations of free and conjugated oxazepam in maternal and fetal plasma were determined by gas/liquid chromatography. In early pregnancy the mean ratio between the plasma concentration of total drug in the umbilical cord and a maternal vein was 0.6, whereas in late pregnancy, the ratio was 1.1. Both in early and late pregnancy, the free and glucuronide conjugate of oxazepam were found in the fetus at concentrations which indicate transplacental passage of the parent drug and its metabolite. There was great interindividual variation in the plasma levels both of free and conjugated oxazepam. 27 references. (Author abstract modified)

**003766** Kosten, Thomas R.; Camp, Walter. Yale-New Haven Hospital, Dana Psychiatric Clinic, 589 Howard Ave., New Haven, CT 06510 **Inappropriate secretion of antidiuretic hormone in a patient receiving piperazine phenothiazines.** Psychosomatics. 21(4):351, 354, 355, 1980.

A case report which documents the syndrome of inappropriate antidiuretic hormone secretion (SIADH) and seizures from water intoxication in a woman recently placed on a low dosage of a piperazine phenothiazine is presented. She was taking no other drugs known to be associated with SIADH and the syndrome resolved on discontinuation of this medication. It is suggested that polydipsia in a patient receiving piperazine phenothiazines may be quite dangerous. Monitoring of patients on this type of drug for hyponatremia is recommended. 14 references.

**003767** Lechin, Fuad,; Van Der Dijs, Bertha. Apartado 80.983, Caracas 108, Venezuela **Effects of dopaminergic blocking agents on distal colon motility.** Journal of Clinical Pharmacology. 19(10):617-625, 1979.

The dopaminergic blocking agents haloperidol, sulpiride, pimozide, and thioridazine were all able to modify motility of the distal colon in human Ss. Haloperidol and sulpiride induced different and frequently antagonistic responses, depending on the preexisting pattern of motility. Biperiden, a centrally acting anticholinergic drug, antagonized the rebound of motility induced by sulpiride in high intestinal tone Ss. Similar results were seen with dihydroergotamine, an adrenergic blocker, in low intestinal tone Ss. Results show that clinically useful antidopaminergic agents may alter.distal colon motility in humans. 56 references.

**003768** Martin, Joan C.; Martin, Donald D.; Radow, Barbara; Day, Heather E. Dept. of Psychiatry and Behavioral Sciences, University of Washington, Seattle, WA 98195 **Life span and pathology in offspring following nicotine and methamphetamine exposure.** Experimental Aging Research. 5(6):509-522, 1979.

Lifespan and pathology were examined in 79 primiparous rats which received s.c. injections of nictoine (3 mg/kg), methamphetamine HCL (5 mg/kg), or saline (5 mg/kg), or received no injections during the 21 day gestation and 19 day nursing period. Male offspring were divided into three groups at weaning: autopsy animals (n=80) were sacrificed at selected periods over the life-span; aging animals (n=60) were weighed monthly until death; and behavioral animals (n=48) were monitored on a variety of behavioral tasks throughout their life-span. Measures reported include life-span data, organ pathology, and tumor formation. Significant differences were found among the four offspring groups for tumor incidence, gross pathology, and age at death for the autopsy group, and weight maintenance for the aging group. 13 references. (Author abstract modified)

**003769** Melamed, Eldad. Dept. of Neurology, PO Box 499, Hadassah University Hospital, Jerusalem, Israel **Early-morning dystonia: a late side effect of long-term levodopa therapy in Parkinson's disease.** Archives of Neurology. 36(5):308-310, 1979.

Four women with Parkinson's disease undergoing prolonged levodopa therapy, who suffered daily early morning episodes of dystonic posturing affecting one lower extremity, several years after initiation of treatment, are described. The dystonia occurred only in the early morning, on awakening, and before the first dose of levodopa, when the patients were in the akinetic/rigid state with no dyskinesias. It further interfered with gait, slowly subsided within 1 to 2 hours, and did not recur until the next morning. This abnormal involuntary posture was unaffected by manipulations of daily levodopa dosage and schedule, completely disappeared after withdrawal of drug therapy, and recurred following its readministration. Additional adverse reactions including dyskinesias, phenomena, and declining efficacy of levodopa were present in all patients. Early morning dystonia may represent another late side-effect secondary to long-term levodopa administration in parkinsonism. 19 references. (Author abstract)

**003770** Miller, Russell R.; Greenblatt, David J. Boston Collaborative Drug Surveillance Program, 400 Totten Pond Road, Waltham, MA 02154 **Clinical effects of chloral hydrate in hospitalized medical patients.** Journal of Clinical Pharmacology. 19(10):669-674, 1979.

Of 26,294 hospitalized medical patients monitored in the Boston Collaborative Drug Surveillance Program, 5,435 (21%) were given chloral hydrate. The drug was prescribed almost exclusively for insomnia and was more often given in combination with benzodiazepine anxiolytics than with other psychotropic drugs. Unsatisfactory therapeutic response to chloral hydrate was reported for 15% of those receiving it. Adverse actions were attributed to chloral hydrate in 119 patients (2.2%). CNS depression was the most common side-effect, followed by sensitivity reactions, gastrointestinal disturbances, and CNS excitation. CNS depression occurred more often with a 1.0g dose than with a 0.5g dose, in patients more than 50 years old, in patients treated concurrently with a benzodiazepine, and in patients with elevated blood urea nitrogen levels upon admission. It is concluded that the safety and efficacy of chloral hydrate justify its continued used in hospitalized patients. 6 references.

**003771** Mumenthaler, M.; Kaeser, H. E.; Meyer, A.; Hess, T. University Dept. of Neurology, Inselspital, CH-3010 Berne, Switzerland **Transient global amnesia after clioquinol: five personal observations from outside Japan.** Journal of Neurology, Neurosurgery, and Psychiatry. 42(12):1084-1090, 1979.

Five personal observations of an acute amnestic episode in younger individuals after intake of clioquinol are described together with three observations from the medical literature. In five of these cases, the episode began after an unusually large dose, in three cases, after a therapeutic dose with a latency of about 24 hours. The clinical aspect closely resembled classical transient global amnesia but the episode after clioquinol lasted longer (24 hours to 3 days) and a more or less extensive retrograde amnesia persisted permanently. In one patient, after three tablets of Mexase, a clioquinol concentration of 12 mcg/ml in plasma was found 24 hours after the specified dose, which is an unexpectedly high concentration compared to those reported as late as 24 hours after a single equal dose of Mexase or any other clioquinol containing preparation. Another patient had a brief relapse 2 years after the first episode, after a single therapeutic dose of another clioquinol preparation. 27 references. (Author abstract)

**003772** Nation, Roger L. Foundation 41, Women's Hospital, Crown St. Surry Hills, New South Wales 2010, Australia **Drug kinetics in childbirth.** Clinical Pharmacokinetics. 5(4):340-364, 1980.

The physiological adjustments that occur in childbirth and their possible consequences on drug kinetics are considered in a review of pharmacokinetic studies. The rate of drug absorption from the gastrointestinal tract may be normal in labor, provided that narcotic analgesics are not administered concurrently. Altered blood flow characteristics in the extremities could modify drug absorption. Drug distribution might be altered as a result of the presence of placental fetal tissues. Uterine contractions, maternal posture, and obstetric medication have been found to affect the extent of some of the physiological changes that occur. All of these drugs are capable of crossing the placenta to some degree. The fetal exposure to, and neonatal burden at delivery of drugs administered during labor and delivery may be influenced by many factors including maternal posture, mode of drug administration, the drug administration to delivery interval, fetal pH, and whether intravenous bolus drug administration coincides with the contraction or relaxation phase of uterine activity. It is concluded that drug effects should be of considerable importance in the clinical management of the newborn. 159 references. (Author abstract modified)

**003773** Ochs, Hermann R.; Greenblatt, David J.; Harmatz, Jerold S.; Bodem, Gunther. Medizinische Universitatsklinik, Kardiologie, 53 Bonn-Venusberg, Bonn, Germany **Serum digoxin concentrations and subjective manifestations of toxicity.** Pharmacology. 20(3):149-154, 1980.

The relation of serum digoxin concentrations (SDC) to subjective manifestations of toxicity was evaluated in 300 patients treated chonically with a glycoside preparation (beta-acetyldigoxin, beta-methyldigoxin, digoxin, or lanatoside-C). Daily glycoside doses correlated poorly with steady-state SDC. Subjective symptoms of gastrointestinal, neuromuscular, and psychiatric toxicity tended to increase with increase SDC, but the trends were not significant. 12 references. (Author abstract modified)

**003774** Peck, Valerie; Shenkman, Louis. Shenkman: Endocrine Unit, Dept. of Medicine, New York University Medical Center, 550 First Ave., New York, NY 10016 **Haloperidol-induced syndrome of inappropriate secretion of antidiuretic hormone.** Clinical Pharmacology and Therapeutics. 26(4):442-444, 1979.

Clinically significant hyponatremia was observed on two occasions in a male patient being treated with haloperidol for chronic schizophrenia. This patient was unable to excrete a water load while on haloperidol, but showed normal ability when not on the drug. It is concluded that haloperidol interfered with the excretion of a water load and induced inappropriate secretion of antidiuretic hormone. 11 references. (Author abstract modified)

**003775** Petty, Leonora K.; Spar, Carol J. Neuropsychiatric Institute, University of California, 760 Westwood Plaza, Los Angeles, CA 90024 **Haloperidol-induced tardive dyskinesia in a 10-year-old girl.** American Journal of Psychiatry. 137(6):745-746, 1980.

A case study is reported of a 10-year-old girl who exhibited tardive dyskinesia symptoms related to her haloperidol therapy. The child had received antipsychotic medications for 4 years and during this time of treatment her symptoms of tardive dyskinesia worsened when haloperidol was continued. She exhibited oral dyskinesia as well as choreoathetoid movements involving the head and trunk. She was hospitalized, taken off all medication, and was treated with behavioral therapy for the control of her psychotic symptoms. This case highlights the dangers of treating children with antipsychotic drugs. 4 references.

**003776** Pfeiffer, Carl C.; Papaioannou, Rhoda; Sohler, Arthur. Brain Bio Centre, Princeton, NJ 08540 **Effect of chronic zinc in-**

**toxication on copper levels, blood formation and polyamines.** Journal of Orthomolecular Psychiatry. 9(2):79-89, 1980.

Laboratory findings from a 20-year-old woman who had been taking between 440 and 5700 mg of elemental zinc, or an average of 2300 mg every day for 4 months are reported. A serum zinc level of 1160 mcg/dl, a serum copper of 8 mcg/dl and undetectable ceruloplasmin were the most striking findings. The patient had previously gone through an acute anxiety state and a brief period of psychosis at age 15. She spent 3 months in a psychiatric hospital at age 16 and was diagnosed as pyroluric early in her college career. Multivitamin therapy successfully alleviated the symptoms, but she discontinued all treatment shortly thereafter and was discharged from college being completely psychotic and violent. The zinc overdose was administered by her parents in the hope of managing her psychosis. Successful treatment involved oral copper therapy and cessation of excess zinc, along with generous supplements of vitamin-C. 33 references. (Author abstract modified)

**003777** Pollack, Michael A.; Burk, Peter G.; Nathanson, Gerald. Montefiore Hospital, 111 E. 210th St., Bronx, NY 10467 **Mucocutaneous eruptions due to antiepileptic drug therapy in children.** Annals of Neurology. 5(3):262-267, 1979.

Three children with bullous erythema multiforme and one with toxic epidermal necrolysis associated with antiepileptic drug therapy are described. One patient showed seven mucocutaneous eruptions caused by three classes of antiepileptic drugs. Lymphocyte stimulation by antiepileptic drugs could not be demonstrated in two patients on whom the appropriate studies were performed, and no precipitating antibodies to antiepileptic drugs were found. Diagnostic and therapeutic principles that may reduce the incidence of life threatening mucocutaneous eruptions are outlined. 27 references. (Author abstract modified)

**003778** Portnoi, Valery A. Division of Geriatric Medicine, George Washington University Medical Center, Washington, DC 20037 **Digitalis delirium in elderly patients.** Journal of Clinical Pharmacology. 19(11 and 12):747-750, 1979.

Case histories of four elderly patients with CNS signs of digitalis toxicity (mental function deterioration) wherein the psychiatric complications of digoxin therapy were early or the only signs of digitialis toxicity, are presented. Evidence of toxicity included lethargy, depression which was not present previously, confusion, restlessness, emotional instability, hyperventilation, and vertigo. Vomiting developed 4 days after the onset of the mental changes, but no cardiac arrhythmias were observed. Three of the four patients recovered, with a return of their mental status to the pretoxic state. It is noted that in the elderly, the recognition of psychotic signs of digitalis toxicity is frequently made difficult by the presence of other psychiatric problems. 13 references.

**003779** Rosenbaum, A. H.; De La Fuente, J. R. Dept. of Psychiatry, Mayo Clinic, Rochester, MN 55901 **Benzodiazepines and tardive dyskinesia.** Lancet. No. 8148:900, 1979.

In a letter to the editor, evidence is presented to emphasize that the use of benzodiazepines in the treatment of tardive dyskinesia (TD) is controversial at best and that these agents might worsen and/or even induce dyskinesia-like symptoms. Observations of six patients with TD are reported who presented a clear temporal association between the use of benzodiazepines and the development of dyskinetic movements. If, as it is suggested, affective disorders predispose to TD when treated with neuroleptics, it is considered reasonable to suppose that some of these patients might be at-risk of a similar syndrome or of exacerbation of a preexisting one if they are treated with benzodiazepines. It is recommended that further studies of the involvement of drugs in the pathogenesis of TD are needed but the justification for the use of benzodiazepines in this condition is not strong. 8 references.

**003780** Scharf, Martin Barnett. Pennsylvania State University **Neuropharmacologic and electrophysiologic correlates of rebound insomnia, a benzodiazepine withdrawal syndrome. (Ph.D. dissertation).** Dissertation Abstracts International. 40(1):193-B, 1979. Ann Arbor, Univ. Microfilms No. 7915737, 167p., 1979.

The hypothesis that abrupt withdrawal of certain benzodiazepine drugs would result in rebound insomnia was investigated. Studies in a sleep laboratory in human subjects are cited which demonstrated that rebound insomnia occurred following the withdrawal of four benzodiazepine drugs. Studies of benzodiazepine receptors in rat brain demonstrated that extended administration of short and intermediate acting benzodiazepine drugs increased the number of available receptor binding sites without changing affinity of drug for receptor. It is theorized that a lag in the production and replacement of endogenous benzodiazepine-like compounds produces rebound insomnia. It is suggested that use of benzodiazepines with long-acting metabolites would lessen effects of drug withdrawal, giving the body time to restore endogenous benzodiazepine-like compounds. (Journal abstract modified)

**003781** Shenoy, Ramakrishnan S. Mental Hygiene Clinic, McGuire V. A. Hospital, Richmond, VA **Nocturnal enuresis caused by psychotropic drugs.** American Journal of Psychiatry. 137(6):739-740, 1980.

Two case studies are reported of two young men diagnosed as schizophrenic, who developed nocturnal enuresis following treatment with thioridazine or thiothixene. Neither of the men had any history of genitourinary abnormalities. The nocturnal enuresis was controlled by having the patients take their medication in the morning and limiting their nighttime intake of fluids. Possible mechanisms causing the enuresis are discussed. 7 references.

**003782** Sherman, Richard A. Audie L. Murphy Veterans Hospital, San Antonio, TX **Successful treatment of one case of tardive dyskinesia with electromyographic feedback from the masseter muscle.** Biofeedback and Self-Regulation. 4(4):367-370, 1979.

Evidence from one case with a 15 month followup is presented to support the conclusion that electromyographic (EMG) feedback from the masseter was effective in controlling tardive dyskinesia. The patient was a 44-year-old White male with a history of more than 20 years of chronic alcohol and multiple drug abuse as well as prolonged use of chlorpromazine and a 5 year history of tardive dyskinesia. A combination of EMG feedback from the frontalis and verbal muscle relaxation training were not effective in this cases. 6 references. (Author abstract modified)

**003783** Singer, L.; Imbs, J.-L.; Singer, P.; Danion, J.-M. Service de Psychiatrie II du C.H.U. de Strasbourg, F-67005 Strasbourg Cedex, France **/Favorable development of a nephrotic syndrome occurring in spite of continued lithium treatment./** Evolution favorable d'un syndrome nephrotique malgre la poursuite d'un traitement par le lithium. Annales Medico-Psychologiques. 137(6-7):584-589, 1979.

Favorable development of a nephrotic syndrome was observed during lithium therapy applied successfully to a 58-year-old patient suffering from manic-depressive psychosis. The development of the nephrotic syndrome was favorable, while the patient was under observation for almost a year. This result is in contrast with several recent publications which stressed the ap-

pearance of nephropathy in the course of lithium therapy. It is concluded that only a systematic study of the development of kidney functions during prolonged lithium therapy of a group of patients which would be as homogenous as possible could determine renal tolerance of lithium. A discussion follows the text of the article. 5 references. (Journal abstract modified)

**003784** Snow, S. Steve; Logan, Thomas P.; Hollender, Marc H. Vanderbilt University Hospital, Nashville, TN 37232 **Nasal spray** British Journal of Psychiatry. 136(March):297-299, 1980.

A case history is described of a 26-year-old patient who was toxic psychosis. The patient said she had difficulty breathing and feared she would smother without the nasal spray, which she used every 15 minutes. When admitted to the hospital for depression and suicidal impulses, she was also experiencing visual and tactile hallucinations, visual illusions, and paranoid delusions. A neurological examination revealed no abnormalities. These symptoms receded after the nasal spray was discontinued. Similar case studies are cited, and possible mechanisms for these occurrences are suggested. 4 references.

**003785** Solomon, Jonathan G. 2101 Executive Dr., Hampton, VA 23666 **Lithium toxicity precipitated by a diuretic.** Psychosomatics. 21(5):425, 429, 1980.

The case of a manic-depressive patient who took a diuretic without her physician's knowledge resulting in depletion of potassium and hyperlithemia with neuromuscular side-effects is reported. An atypical presentation without the usual early symptoms of lithium intoxication is described. Treatment of hyperlithemia is discussed. The need for the physician to educate the patient to become an informed drug consumer who understands drug interactions, dietary restrictions, and the nature of adverse side-effects is pointed out. 19 references.

**003786** Steiner, M.; Elizur, A.; Davidson, S. Mental Health Research Institute, University of Michigan, Ann Arbor, MI 48109 **Behavioral toxicity: neuroleptic-induced paradoxical behavioral toxicity in young borderline schizophrenics.** Confinia Psychiatrica. 22(4):226-233, 1979.

Nine young borderline schizophrenics who developed an acute paradoxical behavioral toxicity as a reaction to the initiation of antipsychotic medication are described. The dynamics, the psychological issues, as well as some possible psychopharmacological interactions are discussed. It is concluded that the risk of behavioral toxicity should not be overlooked or underestimated and the occurence of this reaction must be carefully differentiated from other drug-induced reactions. 31 references. (Author abstract modified)

**003787** von Knorring, Lars; Johansson, Folke. Dept. of Psychiatry, Umea University, S-901 85 Umea, Sweden **Visual evoked potentials as a predictor of reported side effects during a trial of zimelidine vs. placebo in chronic pain patients.** Psychiatry Research. 1(3):225-230, 1979.

Visual evoked potentials were studied in patients before, during, and after a double-blind controlled study of zimelidine, a new, rather specific inhibitor of serotonin uptake in patients with chronic pain. No significant difference in side-effects was found between the zimelidine and placebo groups. Nor was there a significant relationship between the blood levels of the active drug or its metabolite and the frequency of side-effects. Instead, a significant relationship was found in the total group between the frequency of side-effects and the tendency to react with an increase in maximum amplitude of the evoked potentials when stimulus intensity was increased. The same trend was clear in both the zimelidine group and in the placebo group. It is concluded that the augmenting/reducing response in visual evoked potentials seems to be a predictor of the side-effects reported irrespective of the drugs given. 15 references. (Author abstract modified)

**003788** Waziri, Rafiq. Dept. of Psychiatry, University of Iowa, College of Medicine, Iowa City, IA **Lateralization of neuroleptic-induced dyskinesia indicates pharmacological asymmetry in the brain.** Psychopharmacology. 68(1):51-53, 1980.

The lateralization of dyskinesias in psychiatric patients on long-term neuroleptic therapy suggested a pharmacological asymmetry in the brain. In seven of eight right handed patients studied, the drug-induced dyskinesia was greater on the right side than on the left. Results indicate that the basal ganglia in the left or dominant hemisphere are more likely to be affected by neuroleptics than those on the right or nondominant hemisphere. 10 references. (Author abstract modified)

**003789** Wharton, Ralph N. Dept. of Psychiatry, Columbia-Presbyterian Medical Center, 622 West 168th St., New York, NY 10032 **Accidental lithium carbonate treatment of thyrotoxicosis as mania.** American Journal of Psychiatry. 137(6):747-748, 1980.

A case history of a young woman with possibly chronic thyrotoxicosis, who was misdiagnosed as having a manic-depressive illness, is reported. An an adolescent she was treated over a 5 year period with lithium carbonate. Drug treatment for thyrotoxicosis was effective. The use of lithium carbonate, which was been effective in some cases of thyrotoxicosis, is debated.

**003790** Whitloc, F. A.; Bonfield, A. R. Dept. of Psychiatry, University of Queensland, Royal Brisbane Hospital, Brisbane, Queensland 4029, Australia **Propranolol psychosis.** Medical Journal of Australia. 1(4):184-185, 1980.

A case which illustrates typical features of a schizophrenic-like psychoses which may develop in patients being treated for hypertension with propranolol is presented. The patient had grandiose ideas and delusional beliefs and had been taking propranolol (80mg twice daily) for hypertension. After 10 days of observation with no improvement the propranolol medication was stopped and the psychotic symptoms disappeared within 6 days. Whether these hallucinatory states are caused by propranolol alone or by interaction with other drugs and alcohol cannot be decided at present but it is suggested that if propranolol is to be used with phenothiazines to treat schizophrenic psychoses, it might be wise to caution the patient not to drink alcohol while taking these drugs. 7 references.

**003791** Yasuhara, Hajime; Dujovne, Carlos A.; Ueda, Issaku. Dujovne: University of Kansas Medical Center, College of Health Sciences and Hospital, Kansas City, KS 66103 **Relationship between surface activity and toxicity to Chang liver cultures of tricyclic antidepressants.** Pharmacology. 18(2):95-102, 1979.

The cytotoxicities of chlorimipramine (CIM), nortriptyline (NT), amitriptyline (AT), imipramine (IM), and doxepin (SOX) were determined in Change liver cell cultures by measuring cytopathic changes and the loss of enzymes into surrounding media. Time and concentration related cytotoxic effects were found for all five tricyclic antidepressants, with the following decreasing order of cytotoxic potency: CIM, NT, AT, IM, DOX. All the drugs lowered the surface tension of the salt solution contained in the tissue culture media, and the order of surface activity was identical to that obtained for cytotoxicity. It is suggested that the cellular toxicity induced by tricyclic antidepressants in vitro is related to a function of their surface activity. 25 references. (Author abstract modified)

## 16 METHODS DEVELOPMENT

**003792** Fischer-Cornelssen, K. A.; Abt, K. Clinical Research, Sandoz Ltd., CH-4002 Basel, Switzerland **Videotape recording in psychiatry and psychopharmacology: review and presentation of a new method.** Acta Psychiatrica Scandinavica. 61(3):228-238, 1980.

After a review of publications concerning the use of television in psychiatry, a new method of audiovisual evaluation of psychotropic drugs is demonstrated: Standardized Audiovisual Psychiatric Evaluation (SAPE). The procedure requires a pretreatment and posttreatment videotaped interview with each patient. These interviews are later rated and scored by 10 to 20 or more raters using a symptom checklist. Data are evaluated by a fully automated computer program in four steps. Eleven advantages of the method are noted and discussed. 22 references. (Author abstract modified)

**003793** Fouda, Hassan G.; Hobbs, Donald C.; Stambaugh, John E. Dept. of Pharmacology, Thomas Jefferson University, Philadelphia, PA 19107 **Sensitive assay for determination of hydroxyzine in plasma and its human pharmacokinetics.** Journal of Pharmaceutical Sciences. 68(11):1456-1458, 1979.

An assay suitable for hydroxyzine determination in human plasma following therapeutic doses was developed. The method involves gas/liquid chromatography and chemical ionization mass spectrometry of the acetate derivatives of hydroxyzine and of a pentadeuterated analog internal standard. Following administration of single oral 100mg doses to normal male volunteers, peak plasma concentrations of about 80ng/ml were observed. The half-life of drug removal was about 3 hours. 15 references. (Author abstract modified)

**003794** Frey, L. G.; Winter, J. C. Winter: Dept. of Pharmacology and Therapeutics, School of Medicine, State University of New York, Buffalo, NY 14214 **Discriminative stimulus properties of intravenous morphine in the rat.** Psychopharmacology. 66(3):263-266, 1979.

Whether the intravenous route of administration of morphine qualitatively influences the discriminative stimulus effect of morphine in the rat was studied. Using a single lever operant task, rats were trained to discriminate between the effects of 1mg/kg morphine and saline administered intravenously 15 minutes prior to sessions. Tests of stimulus control indicated that responding appropriate to the morphine training treatment was present at 5 minutes and persisted for at least 60 minutes following intravenous administration. Morphine administered 15 minutes prior to sessions resulted in dose related responding with 6mg/kg producing stimulus control not significantly different from the intravenous training treatment. Results suggest that the discriminative stimulus properties of morphine in the rat are qualitatively similar following intraperitoneal and intravenous administration. 17 references. (Author abstract modified)

**003795** Hackett, L. P.; Dusci, L. J. Toxicology Dept., State Health Laboratories, Perth, Western Australia **The use of high-performance liquid chromatography in clinical toxicology. II. Tricyclic antidepressants.** Clinical Toxicology. 15(1):55-61, 1979.

A rapid procedure for the quantitative estimation of steady-state plasma levels is reported. The method described allows as amitriptyline, nortriptyline, imipramine, desipramine, protriptyline, trimipramine, doxepin, and dibenzepin to be estimated rapidly from subtherapeutic to overdose levels. An identical extraction and detection procedure is used for all these drugs. The results obtained were reproducible and the recoveries were good. It is concluded that a method of high performance liquid chromatography has been developed that enables the detection and analysis of tricyclic antidepressants. 13 references. (Author abstract modified)

**003796** Heinze, H.-J.; Kunkel, H. Kunkel: Medizinische Hochschule Hannover, Karl-Wiechert-Allee 9, D-3000 Hannover 61, Germany **The significance of personality traits in EEG evaluation of drug effects.** Pharmakopsychiatrie Neuro-Psychopharmakologie. 12(2):155-164, 1979.

In a paper presented to the 1978 symposium Pharmaco-Electroencephalography," held in Basel Switzerland, the significance of personality traits in EEG evaluation of drug effects are discussed and illustrated with empirical data. It is suggested that the relatively clear and compact picture of an EEG classification of psychotropic substances becomes extremely more complex if the influence of personality traits and topographic differentiations in the EEG are taken into account. Using the example of EEG alterations under diazepam, amitriptyline, pyritinol, EMD 21-657, and caffeine, the complex structure of substance effects, personality factors, topographical differentiations, placebo reactivity, and spontaneous circadian variability of the EEG is demonstrated. 13 references. (Author abstract modified)

**003797** Herrmann, W. M.; Fichte, K.; Itil, T. M.; St. Kubicki. Dept. of Clinical Neuropsychopharmacology, Schering AG, D-1000 Berlin/Bergkamen, Germany **Development of a classification rule for four clinical therapeutic psychotropic drug classes with EEG power-spectrum variables of human volunteers.** Pharmakopsychiatrie Neuro-Psychopharmakologie. 12(1):20-34, 1979.

An objective rule for the classification of psychotropic substances with EEG power spectrum variables is described. Classification is based on data from five simultaneous studies involving 75 healthy volunteers who ingested 20 different psychotropic drugs and five placebos in single oral dosages. Each S took one psychostimulant, one antidepressant, one neuroleptic, one minor tranquilizer, and one placebo in a double-blind, Latin square, crossover design. The discriminant variables are six frequency bands, based on power spectrum estimates and determined by factor analysis, plus total power in the 1.5 to 30.0 Hz range. The objective classification rule was established by multigroup (five groups) linear discriminant analysis. Reclassification of the substances by the new rule yielded correct results for 17 out of 20 psychotropic drugs and four out of five placebos. 40 references. (Author abstract modified)

**003798** Hunt, Peter; Husson, Jean-Marc; Raynaud, Jean-Pierre. Centre de Recherches Roussel Uclaf, F-93230 Romainville, France **A radioreceptor assay for benzodiazepines.** Journal of Pharmacy and Pharmacology. 31(7):448-451, 1979.

A radioreceptor assay for determining benzodiazepines in serum based on the displacement by the drug of specific (3H)diazepam binding to a membrane fraction from rat brain, is described. The limit of detection for clinically active benzodiazepines is about 0.5ng. The parent benzodiazepine and clinically active metabolites can both be measured by this method. This technique was used successfully to assay diazepam, nitrazepam, clobazam, and the novel imidazolobendiazepine HR-158 in human serum following a single oral drug dose. 16 references. (Author abstract modified)

**003799** Itil, Turan M.; Shapiro, D. M.; Herrmann, W. M.; Schulz, W.; Morgan, V. 150 White Plains Road, Tarrytown, NY 10591 **HZI systems for EEG parametrization and classification of psychotropic drugs.** Pharmakopsychiatrie Neuro-Psychopharmakologie. 12(1):4-19, 1979.

The EEG effects of twenty, clinically most frequently used psychotropic drugs and five placebos were studied in 75 male volunteers in five simultaneous studies using the HZI EEG drug

classification system. In each of the studies, single oral doses of five drugs (well known representatives of neuroleptics, antidepressants, anxiolytics, and psychostimulants, as well as placebos) were investigated in 15 Ss in a double-blind, Latin square research design using the methods of the quantitative pharmaco EEG. Results demonstrate that the therapeutically equivalent effective compounds also have similar effects on human EEG. With a classification rule based on discriminant function analysis, 20 of 25 drugs could be classified into the correct clinical therapeutic psychotropic drug group, whereas with a classification rule based on correlation statistics, 19 of the 25 drugs could be so classified. It is suggested that computer analyzed EEG is an important tool in predicting and describing psychotropic properties of compounds, and that it should be used in psychotropic drug development. 51 references. (Author abstract modified)

**003800** Kales, Anthony; Scharf, Martin B.; Soldatos, Constantin R.; Bixler, Edward O. Sleep Research and Treatment Center, Pennsylvania State University College of Medicine, Hershey, PA **Clinical evaluation of hypnotic drugs: contributions from sleep laboratory studies.** Journal of Clinical Pharmacology. 19(7):329-336, 1979.

The contributions of traditional clinical trials and of sleep laboratory studies in the evaluation of hypnotic drugs are discussed. Traditional clinical trials permit the evaluation of large numbers of subjects and of specific target groups, whereas sleep studies permit a more rigorous profile of drug activity. The Guidelines for the Clinical Evaluation of Hypnotic Drugs recently published by the Food and Drug Administration emphasizes the complementary utilization of both types of studies. 44 references.

**003801** Kelly, Raymond C.; Anthony, Robert M.; Krent, Lauren; Thompson, W. Leigh; Sunshine, Irving. Bio-Science Laboratories, 7600 Tyrone Ave., Van Nuys, CA 91405 **Toxicological determination of benzodiazepines in serum: methods and concentrations associated with high-dose intravenous therapy with diazepam.** Clinical Toxicology. 14(4):445-457, 1979.

A procedure for the determination of serum benzoidiazepine levels is described. The procedure involves the extraction of five common benzodiazepines from buffered serum samples, separation of phases by centrifugation, and gas chromatography. The drugs are identified by comparison with simultaneously processed standard samples. A case study is presented to illustrate the application of the technique. The technique was applied to sequential samples drawn from a patient being treated for delirium tremens with large intravenous doses of diazepam. Serum concentrations several times higher than therapeutic concentrations were observed. 19 references. (Author abstract modified)

**003802** Marshall, Elizabeth F. Research Unit in Psychiatry, University of Newcastle upon Tyne, 11 Framlington Place, Newcastle-upon-Tyne NE1 7RU, England **Monoamine oxidase inhibitors and whole blood, platelet and plasma monoamine oxidase.** Progress in Neuro-Psychopharmacology. 3(4):391-393, 1979.

A method for measuring platelet and plasma monoamine oxidase (MAO) activities from a single whole blood sample is described. By measuring MAO activity in whole lysed blood in the presence of 0.0001M pargyline, it is possible to derive values for whole blood, platelet, and plasma MAO activities. This method is rapid and does not require physical separation of blood fractions. 6 references. (Author abstract modified)

**003803** Matousek, M.; Petersen, I. Klin. Neurofys. Lab. Sahlgrenska sjukhuset, S-41345 Goteborg, Sweden **Automatic measurement of the vigilance level and its possible application in psychopharmacology.** 12(2):148-154, 1979. Pharmakopsychiatrie Neuro-Psychopharmakologie.

A study designed to separate specific EEG effects of psychopharmaca from changes produced by drowsiness is reported in a paper presented to the 1978 symposium Pharmaco-Electroencephalography," held in Basel, Switzerland. The study was based on quantitative evaluation of vigilance level during 5 min of EEG recording under standardized conditions. The equation for computing vigilance level from EEG spectra was obtained by using a training material. The segments were classified visually either as alert EEG or EEG marked by drowsiness. As confirmed by independent test material, the coefficients derived by means of multiple linear regression were applicable to other EEGs for estimating vigilance level. This procedure was used in the evaluation of treatment with baclofen. It is concluded that the specific EEG drug profiles were influenced by the accompanying drowsiness, but the main information was still preserved. In contrast to the specific drug effect, the drug-induced sleep activity could be isolated from other events and studied separately. It was also found that after a standard stimulation, both the general trend and periodicity of the vigilance fluctuations were closely related to the patient's psychic state. 15 references. (Author abstract modified)

**003804** Peat, Michael A.; Finkle, Bryan S.; Deyman, Mary E. Dept. of Pathology, University of Utah Medical Center, Salt Lake City, UT 84112 **High-pressure liquid chromatographic determination of chlordiazepoxide and its major metabolites in biological fluids.** Journal of Pharmaceutical Sciences. 68(11):1467-1468, 1979.

A simple, isocratic, reversed phase high pressure liquid chromatographic procedure for the determination of chlordiazepoxide and its major metabolites in plasma and urine was developed. Recoveries of 80 to 91% with sensitivity limits of 50ng/mol were obtained for the parent drug and its metabolites. This procedure was used successfully to measure the levels of chlordiazepoxide and its desmethyl metabolite in plasma after oral or intravenous administration. Demoxepam was the most common metabolite detected when urine samples were analyzed by this procedure. 20 references. (Author abstract modified)

**003805** Record, Kenneth E.; Rapp, Robert P.; Young, A. Byron; Kostenbauder, Harry B. Young: Division of Neurosurgery, University of Kentucky College of Medicine, Lexington, KY 40506 **Oral phenytoin loading in adults: rapid achievement of therapeutic plasma levels.** Annals of Neurology. 5(3):268-270, 1979.

An oral phenytoin loading regimen derived from a simple pharmacokinetic model that rapidly provides therapeutic blood concentrations of phenytoin is described. Twenty adult patients were given an average dose of 19.1mg/kg phenytoin, divided into two to four increments and given over 3 to 21 hours. Plasma samples drawn 2 to 22 hours after completion of the loading dose resulted in therapeutic levels, ranging from 8.1 to 18.0mcg/ml. Thus, a regimen in which no increment of the loading dose exceeds 600mg is sufficient to achieve and maintain therapeutic plasma concentrations. 11 references. (Author abstract modified)

**003806** Rosenberg, Larry S.; Van Vunakis, Helen. Dept. of Biochemistry, Brandeis University, Waltham, MA 02254 **Radioimmunoassay for phencyclidine.** Research Communications in Chemical Pathology and Pharmacology. 25(3):547-557, 1979.

A sensitive and specific radioimmunoassay for phencyclidine (PCP) is described. Levels as low as 50pg of PCP can be detected. The specificity of the antisera was confirmed by inhibit-

ing the labeled PCP/anti-PCP reaction with the parent drug, metabolites, and other related compounds. Plasma samples supplemented with PCP can be analyzed directly by this procedure. 19 references. (Author abstract modified).

**003807** Saneto, Russell P.; Srivastava, Satish K.; Werrbach-Perez, Karin; Perez-Polo, J. Regino. Perez-Polo: Gail Borden 436, University of Texas Medical Branch, Galveston, TX 77550 **Lithium uptake at physiological ion concentrations in a human clonal neuroblastoma cell line.** Journal of Neurochemistry. 34(6):1520-1521, 1980.

The use of human clonal neuroblastoma cell line as a model system for the investigation of lithium uptake at physiological ion concentrations is described. Whereas human erythrocytes have been shown to have a ouabain sensitive component, a phloretin sensitive component, and a component of lithium transport not sensitive to either drug, C1300 mouse neuroblastoma cells lack the ouabain sensitive components. At physiological concentration of both sodium and potassium, the SY/5Y human neuroblastoma cells exhibit both a ouabain sensitive and a oubain insensitive component, in contrast to the human erythocytes or C1300 mouse neuroblastoma cells. Results of studies of the effects of the drugs ouabain and phloretin on lithium transport components in the SY/5Y clonal neuroblastoma cell line suggest that the expression of lithium uptake mechanisms in human neuronal cells might be best studied in diploid adrenergic-like human neuroblastoma lines in culture as opposed to nonneuronal tissues, such as erythrocytes or cell lines of nonhuman origin. 12 references.

**003808** Schieffer, Gary W. Pharmaceutical Research Division, Norwich-Eaton Pharmaceuticals, Division of Morton-Norwich Products, Inc., Norwich, NY 13815 **Reversed-phase high-performance liquid chromatographic investigation of levodopa preparations I: amino acid impurities.** Journal of Pharmaceutical Sciences. 68(10):1296-1298, 1979.

A reversed phase high performance liquid chromatographic procedure with ultraviolet detection at 280nm was developed for determination of 6-hydroxydopa, tyrosine, 3-0-methyldopa, and other trace amino acid impurities in levodopa preparations. The method is fast and sufficiently sensitive to determine trace impurities at 0.1% of the levodopa concentration with a relative standard deviation of 4% to 6%. The trace impurities can be estimated at less than 0.01%. 15 references. (Author abstract)

**003809** Schieffer, Gary W. Pharmaceutical Research Division, Norwich-Eaton Pharmaceuticals, Division of Morton-Norwich Products, Inc., Norwich, NY 13815 **Reversed-phase high-performance liquid chromatographic investigation of levodopa preparations II: levodopa determination.** Journal of Pharmaceutical Sciences. 68(10):1299-1301, 1979.

A reversed phase high performance liquid chromatographic procedure with ultraviolet detection at 280nm was developed for levodopa preparations. This stability indicating assay is specific for levodopa with respect to at least five degradation products and five impurities found in pharmaceutical preparations of the drug. The method is fast, permitting the assay of about 25 samples in an 8 hour workday. 14 references. (Author abstract modified)

**003810** Stern, Stephen L.; Rush, A. John; Mendels, J. Depression Research Unit (151E), V.A. Medical Center, University and Woodland Avenues, Philadelphia, PA 19104 **Toward a rational pharmacotherapy of depression.** American Journal of Psychiatry. 137(5):545-552, 1980.

Several approaches that show promise for predicting which antidepressant medication will be best for a particular patient and for achieving maximum benefit from each drug are reviewed. These include delineation of clinical and historical characteristics associated with response to various drugs, use of psychological tests, assessment of biochemical and electroencephalographic parameters, evaluation of mood response to amphetamine, determination of acetylator status, and measurement of plasma tricyclic levels and degree of inhibition of platelet monoamine oxidase. It is concluded that the use of these approaches may improve our ability to help depressed patients. 87 references. (Author abstract)

**003811** Thomas, D. J.; Zilkha, E.; Redmond, Sheila; Du Boulay, G. H.; Marshall, John; Russell, R. W. Ross; Symon, Lindsay. Institute of Neurology and National Hospital for Nervous Diseases, Queen Square, London WC1N 3BG, England **An intravenous 133xenon clearance technique for measuring cerebral blood flow.** Journal of the Neurological Sciences. 40(1):53-63, 1979.

An atraumatic isotope clearance method for measuring cerebral blood flow (CBF) is described. The method employs digital computer analysis following 133xenon. The accuracy of the method was confirmed by comparison with results obtained during the standard intracarotid xenon isotope technique; test/retest reproducibility was also satisfactory. The method has been used successfully in more than 1,400 studies on patients with conditions ranging from recent subarachnoid hemorrhage to chronic dementia. In control Ss, the mean fast component flow was 68.6ml/100g/minute. No difference between the two cerebral hemispheres was found, but flow was higher anteriorly within the hemispheres. A significant inverse correlation was found between CBF and age. 23 references. (Author abstract modified)

# 17 MISCELLANEOUS

**003812** Abt, K. Abt. fur Biomathematik, Fachbereich Humanmedizin, Universitat Frankfurt, Theodor Stern Kai 7, D-6000 Frankfurt/Main 70, Germany **Statistical problems in the analysis of comparative pharmaco-EEG trials.** Pharmakopsychiatrie Neuro-Psychopharmakologie. 12(2):228-236, 1979.

Statistical problems in the analysis of comparative pharmaco-EEG trials are discussed in a paper presented at the 1978 symposium "Latest Advances in Pharmaco-Electroencephalography," held in Basel Switzerland. Already condensed data from the EEG power spectra are assumed. Since in general there is only a limited number of subjects available in a study to evaluate and compare the effects of a number of drugs by EEG, the experimental design is usually of the crossover type. With respect to this design, the requirements for application and for appropriate analysis are stated. Further, the problems are indicated which arise when the number of subjects is not a multiple of the number of drugs and/or when there are missing values. Finally, the topic of repeated null hypothesis testing and the inflation of the overall significance level is treated. Suggestions are made as to how to avoid the indicated problems at the present stage of methodological statistical research. 6 references. (Author abstract modified)

**003813** Annitto, William. P.O. Box 28, Summit, NJ 07901 **Excessive caution in psychotropic dosage.** Psychosomatics. 21(5):433-434, 1980.

A case of a 75-year-old woman suffering from depression who had been treated with clinically ineffective amounts of doxepin is reported. Increase in the dosage of doxepin brought improved sleep and brighter, less irritable mood. Previous concern for cardiovascular complications is acknowledged; however, the patient's mental status is seen as contraindicating a It is argued that, although it can itself be harmful when used as a self-protective rationalization for unwarranted conservatism in choice of treatment modalities and analysis of risk/benefit ratio. 3 references.

**003814** Ban, Thomas A. Tennessee Neuropsychiatric Institute, 1501 Murfreesboro Road, Nashville, TN 37217 **Pharmacological treatment of psychosomatic manifestations in geropsychiatric patients.** Activitas Nervosa Superior. 21(2):116-121, 1979.

The interrelationship between geropsychiatry and psychosomatics is discussed, and the pharmacological treatment of psychosomatic manifestations in geropsychiatry patients is reviewed. It is noted that the frequently encountered stresses of the aged include physical and mental limitations or disabilities, retirement, loss of relatives and friends, and rejections by children. Psychotherapeutic approaches to treatment have increasingly been supplemented or replaced by pharmacological treatments in psychosomatic disorders in old patients. Pharmacological treatments such as anxiolytic sedatives, tricyclic antidepressants, monoamine oxidase inhibitors, and endocrine preparations are discussed. 30 references.

**003815** Bender, W.; Siepmann, K. Psychiatrische Klinik der Universitat Munchen, D-8000 Munich 2, Germany **/Therapeutic stereotypes in psychiatric illnesses./** Therapeutische Stereotypien bei psychiatrischen Erkrankungen. Psychiatria Clinica. 13(1):1-12, 1980.

Using mathematical models described by Overall, therapeutic stereotypes in prescribing psychotropic drugs and their dependence on symptom, syndrome, and diagnostic level were investigated in 301 psychiatric inpatients. The psychotropic drugs are described in a dimensional representation of psychopathology. Besides dependence on patients' characteristics such as age and on clinicians' characteristics such as special orientation, the therapeutic stereotyping was found to be most influenced by the symptom level. Only lithium therapy and electroconvulsive therapy were keyed to diagnosis. Getting more familiar with a psychotropic drug increased indications and contraindications on symptom level and thus, the therapeutic stereotype became more differentiated. Therapeutic stereotypes of German and French psychiatrists were compared and a satisfactory congruence relating to dimensionality and relationships among drugs studied was found. 12 references. (Journal abstract modified)

**003816** Burgess, Helen A. Yale University School of Nursing, New Haven, CT **When a patient on lithium is pregnant.** American Journal of Nursing. 79(11):1989-1990, 1979.

The problems nurses face when they have a pregnant patient who is on lithium are discussed. Because lithium crosses the placenta, the fetus is exposed to the same concentration as the mother. Women in childbearing years should therefore be treated with lithium only if they are known manic depressives. If the nurse first meets the woman who is taking lithium during her pregnancy, she can provide guidance about diet and medications that are appropriate for any pregnant woman. She can help to lay the groundwork for good family relationships and give other prenatal information. Postpartum nurses also need to be alert for possible lithium complications. Throughout her pregnancy and the postpartum period, the patient on lithium needs the care of nurses who are alert to signs of possible toxicity and can help her guard against too much stress. 5 references.

**003817** Committee on the Review of Medicines. no address **Systematic review of the benzodiazepines: guidelines for data sheets on diazepam, chlordiazepoxide, medazepam, clorazepate, lorazepam, oxazepam, temazepam, triazolam, nitrazepam, and flurazepam.** British Medical Journal. No. 6218:910-912, 1980.

A systematic review of benzodiazepine therapy is presented which includes: indications for use in treatment of conditions other than anxiety and insomnia, long-term efficacy, residual effects, dependence potential and withdrawal symptoms, implications of differing pharmacological and kinetic properties for clinical practice, and use in the elderly. Both short-acting and long-acting benzodiazepines are covered including diazepam, chlordiazepoxide, medazepam, clorazepate, lorazepam, oxazepam, temazepam, triazolam, nitrazepam, and flurazepam. All of the benzodiazepines were found to be efficacious in the treatment of anxiety and insomnia; additional indications for long-acting benzodiazepine therapy might include muscle spasm, symptomatic treatment of acute alcohol withdrawal, and night terrors and somnabulism in children. The benzodiazepines are not recommended for the treatment of depression, tension headache, psychotic illness, or anxiety and insomnia in children. The long-term efficacy of the sedative hypnotics, including benzodiazepines, is questioned. 2 references.

**003818** Cooper, Alan J. Dept. of Psychiatry, University of Western Ontario, London, Ontario, Canada **Tryptophan antidepressant 'physiological sedative': fact or fancy?** Psychopharmacology. 61(1):97-102, 1979.

Some recent publications relating to the antidepressive and sedative effects of L-tryptophan, the precursor of 5-HT, were reviewed. The evidence suggests that the amino acid is as effective as standard tricyclic drugs in alleviating the symptoms of depression, especially those cases presenting with mainly psy-

chomotor retardation, and is synergistic with monoamine oxidase inhibitors. L-tryptophan would also appear to be a physiological sedative. This action, however, appears to be related to the time of administration and at present has only been demonstrated at night, when endogenous levels of 5-HT are at their peak. In terms of practical therapeutics, L-tryptophan appears to have greater potential as an antidepressant than as a sedative. 67 references. (Author abstract)

**003819** de la Fuente-Ramirez, Juan Ramon. Dept. of Psychiatry and Psychology, Mayo Medical School, Rochester, MN 55901 **/Plasma levels of psychotropic drugs./** Niveles plasmaticos de drogas psicotropicas. Salud Mental. 2(2):30-33, 1979.

Psychotropic medications, particularly neuroleptics and tricyclic antidepressants, are discussed. A common problem in clinical work is the estimation of the dose of these medications which must be administered. An overdose or an underdose is the frequent cause of serious problems in the patient, but a clinical and pharmacological correlation between plasma levels and therapeutic response solves this problem. By determining plasma levels, high and low doses are established, and then can be varied according to the individual patient's needs. If the patient responds adequately to the drug, then the cost of the test is justified. 33 references.

**003820** el-Guebaly, N.; Holmes, L. Dept. of Psychiatry, St. Boniface General Hospital, Winnipeg, Manitoba, Canada **The methadone maintenance experience: its impact on the future of chemical dependency.** Canada's Mental Health. 28(1):15-17, 1980.

Implications from the rise and fall course of the methadone maintenance model for heroin addiction are discussed. The importance of such factors as epidemiological characteristics, multicausality, delivery of service, community acceptance, effect on offspring, evaluation issues, and staff training are emphasized. The methadone maintenance programs in the United States and Canada have been deemphasized in light of modifications in the original treatment philosophy and practice, differences in the amount of psychological or other backup services, differences in the way methadone was used, and differences in the therapeutic ambiance of the treatment centers. The failure of this approach to chemical dependence, however, provides information to planners so that more realistic expectations will be shared by consumers, staff, and society; and the search for more antagonists, long-acting compounds, combination treatments (disulfiram-methadone), or sequential pharmacological treatments will be continued. 18 references.

**003821** Fauman, Michael A. Division of Psychiatric Liaison, Henry Ford Hospital, 2799 West Grand Boulevard, Detroit, MI 48202 **Tricyclic antidepressant prescription by general hospital physicians.** American Journal of Psychiatry. 137(4):490-491, 1980.

The use of tricyclic medication by surgeons and internists in a large private general hospital was examined using a questionnaire completed by 117 physicians. Results show that 61.5% of the physicians used tricyclic medication for treatment of depression, chronic pain, and insomnia, as well as agitation, anxiety, and enuresis. The more effective the medication was rated, the more lifely it was that adequate doses of the medication were prescribed. There was wide variation in the type and number of routine laboratory tests ordered and precautions observed before tricyclic compounds were prescribed. It seems clear that a psychiatric liaison service has an important role in advising physicians on the correct indications for prescription of tricyclic medication. 5 references.

**003822** Ferner, U. Clinical Research, Sandoz Ltd., Lichtstrasse 35, CH-4002 Basel, Switzerland **Some methodological aspects on the statistical analysis of pharmaco-EEG data.** Pharmakopsychiatrie Neuro-Psychopharmakologie. 12(2):220-227, 1979.

Methodological issues in the statistical analysis of pharmaco-EEG data are considered in a paper presented at the 1978 symposium in Basel Switzerland. For testing hypotheses of time and treatment effects and interactions, various parametric and nonparametric approaches are demonstrated with respect to their assumptions and practicality. For parallel group designs, the MANOVA is proposed for comparing profiles of different treatment groups, taking the repeated measurement points as different variables. For analyzing design and the Latin square, with and without grouping effect, are discussed. A steady state condition of the subjects and no prolonged drug effects must be presumed. If the available number of subjects is restricted to the same number as the number of drugs and/or doses to be compared, no appropriate statistical model is known that could deal with testing a multitude of hypotheses with the same set of correlated measurement points and correlated EEG variables. It is therefore recommended not to carry out an inferential statistical analysis for such situations, but rather to render a description of results with special consideration and strict control of all factors which may influence findings, with a special account of their relevance. 12 references. (Author abstract modified)

**003823** Freyhan, Fritz A. 2015 R Street, NW, Washington, DC 20009 **The target symptoms for treatment of depressive illness revisited.** Comprehensive Psychiatry. 20(6):495-501, 1979.

The approach toward the treatment of depression in which the target symptoms of depression are treated psychopharmacologically is reviewed. Symptoms may be defined as those which are behavioral, experiential, and/or somatic. Physicians depend on their diagnostic capability to recognize the symptoms that lend themselves to treatment with a given psychoactive drug. A serious therapuetic problem exists in that some physicians overprescribe and substitute anxiolytics and neuroleptics for potent antidepressants which precludes in most instances satisfactory therapeutic results. Specific treatment for the underlying causes of mood disorders remains hypothetical; therefore, the conceptualization of what represents treatable pathology remains a chief concern. In this regard, the formulation of target symptoms is viewed as an important step towards successful treatment of depression. 12 references.

**003824** Gardos, George. Institute for Research and Rehabilitation, 591 Morton Street, Boston, MA 02124 **Drug treatment of the schizophrenic patient.** Journal of Psychiatric Treatment and Evaluation. 2(1):33-36, 1980.

Some commonly encountered difficulties which face the hospital psychiatrist in dealing with schizophrenic patients are highlighted. An initial history needs to include medical and neurological conditions, drug response in first degree relatives, and a complete drug history. A pragmatic classification of schizophrenia is offered: 1) regular schizophrenia, 2) affective components in schizophrenia, and 3) MBD schizophrenia. The causes of poor response to antipsychotic drug therapy is reviewed, and suitable alternatives are suggested. 3 references. (Author abstract modified)

**003825** Gasser, T. Central Institute of Mental Health, D-6800 Mannheim 1, Germany **Statistical handling of EEG-data.** Pharmakopsychiatrie Neuro-Psychopharmakologie. 12(2):210-219, 1979.

Statistical problems in the handling of EEG data for classificatory and evaluative studies of psychotropic drugs are discussed in a paper presented at the 1978 symposium in Pharmaco-Electroencephalography," held in Basel, Switzerland. Focus is on the treatment of EEG data as time series. More em-

phasis is placed on spontaneous activity than on event related potentials. Smoothing techniques are discussed both for the nonparametric estimation of regression functions and of densities. Some new promising methods are presented. The fundamentals of time series analysis are reviewed, in particular, spectrum analysis. For the difficult areas of parameterization of EEG time series, the desirable characteristics of parameters are compared with the methods already in use. 13 references. (Author abstract modified)

**003826** Georgotas, Anastase; Gershon, Samuel. Dept. of Psychiatry, New York University Medical Center, 550 First Ave., New York, NY 10016 **Biology and pharmacological treatment of depression.** Hillside Journal of Clinical Psychiatry. 2(1):27-39, 1980.

Studies over the last 20 years on the relationship between brain and behavior and the pharmacological treatment of depression are reviewed. Biological studies have clarified the neurobiological mechanisms that underlie both normal and abnormal behavior and have focused specifically on the role of catecholamines and indoleamines, norepinephrine, serotonin, the neuroendocrine system, and genetic factors in the etiology of depression. Pharmacologic research has investigated the effectiveness of tricyclic antidepressants, MAO inhibitors, lithium, and stimulants in the control of unipolar and bipolar depression. Newer advances in pharmacokinetics, especially the application of plasma levels to establish accurate therapeutic monitoring, as well as studies of the role of different hormones in modulating the effects of several neurotransmitters, offer more promise for the future. 49 references.

**003827** Hadsall, Ronald Sven. University of Iowa **Characteristics of psychotropic drug prescribing among primary care physicians. (Ph.D. dissertation).** Dissertation Abstracts International. 40(7):3103-B, 1980. Ann Arbor, Univ. Microfilms No. 7928583, 188p., 1979.

The influences of differing physician characteristics and attitudes on the diagnosis of emotional problems and the prescribing of psychotropic and nonpsychotropic drugs were investigated with 52 community based primary care physicians. After controlling for patient characteristics, there was not a statistically significant relationship between board certification, practice size, or physician age and the rate at which study physicians diagnose emotional problems. Physicians who tend to refer patients with emotional problems had a significantly lower emotional diagnosing rate. Board certification, physician age, physician propensity to prescribe drug therapy, and the feeling that patients expect drug therapy were significantly related to the prescribing of nonpsychotropic drugs. Board certified physicians tend to prescribe nonpsychotropic drugs at a lower rate than nonboard certified physicians. The prescribing of psychotropic drugs was not predictable. It is reported that only the propensity to prescribe drug therapy was significantly related to the rate at which study physicians prescribed psychotropic drugs for their patients. (Journal abstract modified)

**003828** Hartley, Elizabeth J.; Spuhler, Karen; Prasad, Kedar N.; Seeman, Philip. Dept. of Pharmacology, University of Toronto, Toronto M5S 1A8, Canada **A neuroblastoma clone which has dopamine sensitive adenylate cyclase but which lacks stereospecific binding sites for the neuroleptic (3H)spiperone.** Brain Research. 190(2):574-577, 1980.

A cell line from mouse neuroblastoma (NB) cells which contains dopamine sensitive adenylate cyclase but which apparently lacks specific (3H)spiperone binding sites is described. The high concentrations of neuroleptics required to inhibit the binding of (3H)spiperone to the neuroblastoma homogenates were of the order of those required to inhibit the binding of dopamine sensitive adenylate cyclase in homogenates of neuroblastoma and striatal tissue. It appears that dopamine sensitive adenylate cyclase may be present in cells which do not exhibit the characteristics of specific sites for (3H)spiperone binding. It is concluded that such cells would be very convenient for testing the recent hypothesis of Hyttel (1978) that (3H)cis(Z)-flupenthixol may selectively label the dopamine sensitive adenylate cyclase receptor sites. 27 references.

**003829** Hays, Sarah Ellen. Stanford University **The prolactin response to antipsychotic drugs: clinical and preclinical implications. (Ph.D. dissertation).** Dissertation Abstracts International. 40(7):3396-B, 1980. Ann Arbor, Univ. Microfilms No. 8001936, 133p., 1979.

The hypothesis was tested that the prolactin response to antipsychotic drugs may predict an individual's therapeutic responsiveness to a drug before treatment, and may predict the potential antipsychotic potency of new drugs. Results of experiments on seven normal men with injections of haloperidol suggest that individual differences in prolactin response not explained by serum haloperidol concentrations might be due to individual differences in sensitivity of the pituitary dopamine receptors to blockade by haloperidol. In tests of nine antipsychotic and other drugs on female rats, findings indicate that prolactin releasing potency may be a good predictor of clinical potency if the prediction is based on the prolactin releasing activity of the compound in comparison to clinically active drugs of the same chemical classification. It is concluded that the prolactin response to antipsychotic drug promises to be a useful aid in the clinical management of schizophrenic patients and in the development of new antipsychotic drugs. (Journal abstract modified)

**003830** Janssen, Paul A. J.; Colpaert, Francis C. Janssen Pharmaceutical Research Laboratories, B-2340 Beerse, Belgium **The pharmaceutical industry in neuroscience research.** Trends in NeuroSciences. 2(9):I-II, 1979.

Some of the contributions made by the pharmaceutical industry to neuroscience research are reviewed. One major contribution has involved the identification of the structural requirements for binding to opiate binding sites in neural pathways processing nociceptive stimuli. The advent of neuroleptic drugs has allowed researchers to uncover part of the etiology of schizophrenia. Pharmaceutical laboratories have also been involved in the investigation of the cue properties of drugs. Much current research is devoted to receptor binding processes. It is concluded that human disease must be the primary focus of research in the pharmaceutical industry.

**003831** Jessell, T. M.; Kelly, J. S. St. George's Hospital Medical School, London, England **Peptide pathology ... of mice and men.** Nature. 285(5761):131-132, 1980.

Clinical implications of recent research into neuropeptide function are reviewed. Methods for investigation of the distribution of opioid peptide receptors in human tissue and for the location of benzodiazepine receptors within human cerebral and cerebellar cortex are noted, and research based on the premise that a variety of disease states in man are produced by autoantibodies directed against cell membrane receptors is discussed. Other topics include: improvement in the symptomatology of spinocerebellar degeneration following injection of thyrotropin releasing hormone, the role of endorphins in the pathogenesis of shock, the antihypotensive effects of naloxone, and the role of cholecystokinin (CCK) in satiety and the treatment of obesity with CCK.

**003832** Kety, Seymour S. Dept. of Psychiatry, Harvard Medical School, Boston, MA 02115 **The biological substrates of**

**mental illness.** Journal: National Association of Private Psychiatric Hospitals. 11(3):6-12, 1980.

Preclinical and clinical evidence in support of the belief that disturbances in the biological machinery play a significant role in mental disorders is reviewed. This evidence suggests that serious mental illnesses such as schizophrenia or the affective disorders are associated with malfunctioning chemical transmitters and biochemical processes which affect cognition, emotional state, and behavior in definable ways. The concept of the chemical synapse has also provided a basis whereby genetic deviations, metabolic processes involving biogenic amines, changes in the chemical milieu, hormones, and psychotropic drugs can affect psychological processes and may underlie a number of mental disorders. Developments in neurobiology and neuropharmacology, as well as sophisticated chemical techniques, should further demonstrate the involvement of brain chemistry in normal and abnormal behavior in future research. 10 references.

**003833** Kugler, J.; Lorenzi, E.; Spatz, R.; Zimmermann, H. Psychiatr. Klinik der Universitat Munchen, Nussbaumstrasse 7, D-8000 Munich 2, Germany **Drug-induced paroxysmal EEG-activities.** Pharmakopsychiatrie Neuro-Psychopharmakologie. 12(2):165-172, 1979.

Results of a retrospective study involving 680 EEG investigations of drug-induced paroxysmal activities in 593 patients are reported in a paper presented to the 1978 symposium Advances in Pharmaco-Electroencephalography" held in Basel, Switzerland. Drugs were given singly in the majority of cases, combined in others. The proportions of abnormal EEG in the various groups were (in descending order): clozapine 59%, lithium salts 50%, butyrophenone 44%, maprotiline 37%, dibenzepine 32%, levomepromazine and amitriptyline 31%, imipramine 9%, and diazepam 4%. The proportions of paroxysmal discharges (13%) and generalized transient disturbances with groups of slow-waves (16%) were also greatest in the clozapine group. Seizures were observed in three patients treated with maprotiline, twice during clozapine treatment, once during amitriptyline treatment, and once as an accompaniment of lithium intoxication. Paroxysmal EEG activity is probably an indication of metabolic changes in certain neuronal systems (median thalamic nucleus, lower brainstem limbic system); these form the basis of the antipsychotic activities of the agents but may also lead to abnormal spread of generalized seizures. 20 references. (Author abstract modified)

**003834** Lamy, Peter P. School of Pharmacy, University of Maryland at Baltimore, 636 West Lombard Street, Baltimore, MD 21201 **Consider all factors when treating the elderly.** Long Term Care and Health Services Administration. 3(3):194-202, 1979.

Important factors influencing an elderly patient's reactions to his therapeutic regimen are explored. Inherited factors may change the absorption, metabolism, distribution, and excretion of a drug. Diverse societal factors such as race, religion, and diet can also affect a patient's response. In addition, societal factors may have a profound effect on the decision to seek treatment and on the response to disease symptoms. For example, requests for antianxiety drugs may well differ with the coping mechanism exhibited by various ethnic groups. It is concluded that those rendering health services to the elderly must be familiar with and take into consideration the influence on health of behavior, disease presentation, and drug response, along with such varied factors as inherited traits, sociocultural factors, racial and ethnic differences among patients, and economic constraints. 44 references.

**003835** Lamy, Peter P. University of Maryland School of Pharmacy, Baltimore, MD 21201 **Misuse and abuse of drugs by the elderly -- another view.** American Pharmacy. NS20(5):14-17, 1980.

Problems of drug abuse of prescription drugs among the elderly are addressed with implications for geriatric medicine practitioners and other health care providers. Specific areas of concern include: 1) lack of appreciation for effects of primary and secondary aging, 2) inaccurate diagnosis, 3) inaccuracies in drug treatment and use of unnecessary medications, and 4) deliberate overmedication. The physician's attitude also has much to do with rational drug use, as does knowledge by prescribers of the physiology, pharmacology, pharmacokinetics, and toxicology of drugs used for the elderly. Controversial drugs in the treatment of psychological mental dysfunction in the elderly include alcohol and the benzodiazepines, both of which have beneficial effects on personal and interpersonal processes and in the control of emotions and behavioral patterns in certain instances of somatic disease. 10 references.

**003836** Laska, Eugene; Siegel, Carole; Simpson, George. Siegel: Information Sciences Division, Rockland Research Institute, Orangeburg, NY 10962 **Automated review system for orders of psychotropic drugs.** Archives of General Psychiatry. 37(7):824-827, 1980.

A computerized drug review system which both reviews drug orders and notifies clinicians of orders that are considered exceptions to some clinical guidelines is described. The impact of this system in a psychiatric center in which it has been used since December 1975 is examined in terms of the reduction of the percentage of orders of psychotropic drugs that involve polypharmacy or dose range exceptions. The results show a substantial reduction in orders in exception since the implementation of the system. Future developments planned for the system are noted. 12 references. (Author abstract modified)

**003837** Le Douarec, J.-C Institut de Recherche MSD-CHIBRET, 200, boulevard E.-Clementel, F-63000 Clermont-Ferrand, France **/Anorexigenic drugs: experimental study methods, chemical structures, and classification./** Les anorexigenes: methodes experimentales d'etude, structures chimiques et classification. Therapie. 34(2):131-153, 1979.

Experimental study methods, chemical structures, and classification pertaining to anorexigenic drugs are discussed. Short-term studies of these drugs generally involve the exposure of animals to food for a limited period of time during the day, and the ability of the drug to reduce food consumption is observed. Other methods relate to the choice of an appetizing drink, to the study of the feeding cycle, or hoarding behavior. The use of operant conditioning and electrophysiological techniques is limited to investigations of the mechanism of the action of anorexigenic agents. These agents fall into two categories according to their chemical structures: amphetamines and nonamphetamines. Two subdivisions exist: amphetamine acting drugs which work via central catecholaminergic mechanisms or fenfluramine-like drugs which involve serotonin as the mediator in the brain. 78 references. (Journal abstract modified)

**003838** Loga, Slobodan; Ceric, Ismet; Kecmanovic, Dusan. Psihijatrijska klinika **/Psychopharmacology used in resocialization of mental patients./** Psihofarmaci u resocijalizaciji dusevnih bolesnika. Socijalna Psihijatrija. 6(1):51-54, 1978.

Psychopharmacotherapy of mental patients is discussed as a method of resocialization, i.e. as a method of enabling the disabled person to utilize his aptitudes in a social context which is as normal as possible. When acute mental disorders are dampened by strong antipsychotic medication, the patients, particu-

larly schizophrenics, are given other forms of treatment: psychotherapy and sociotherapy. This is done in outpatient clinics. Prolonged use of drugs should not have side-effects at the neurovegetative level or hypnosedative and reductive inhibiting effects at the level of psychomotility. More or less satisfactory results have been obtained by using neuroleptics such as depo-fluphenazine, pimozide, penfluridol, and other psychoactive substances used in prolonged treatment of mental patients. 11 references.

**003839** Matejcek, M. Biological and Medical Research Division, Sandoz Ltd., CH-4002 Basel, Switzerland **Pharmacoelectroencephalography: the value of quantified EEG in psychopharmacology.** Pharmakopsychiatrie Neuro-Psychopharmakologie. 12(2):126-136, 1979.

The value of quantified EEG in psychopharmacology is discussed in a paper presented at the 1978 symposium Pharmaco-Electroencephalography" held in Basel, Switzerland. One of the first routine applications of quantitative EEG analysis was in the field of human psychopharmacology. As early as the 1960s, quantitative techniques, mainly period and amplitude integration analyses or analogue filtering, were successfully applied to EEG data with the aim of quantifying and objectifying changes induced by psychoactive medication. Thus, step by step, a new research field was developed. Using examples, an attempt is made to give a balanced judgment on the value of pharmacoelectroencephalography. Examples include: single dose EEG studies for determining dose and differences in drug reactivity; EEG studies of repeated drug administration; and chronospectrogram analysis in the assessment of spontaneous and drug-induced changes in vigilance (including studies of D-amphetamine and clozapine). 14 references. (Author abstract modified)

**003840** Munson, Martha Little; OLeary, James S.; Locke, Ben Z. Center for Epidemiologic Studies, National Institute of Mental Health, Rockville, MD 20857 **Use and non-use of medication by sufferers of selected symptoms of depression.** Journal of Human Stress. 6(2):20-27, 1980.

The question of what number of people, suffering symptoms of sleeplessness and enervation, would seek relief through the use of medication was studied. Multiple standardization was used to assess the effects of race, sex, age, marital status, and socioeconomic status on the proportions of people reporting each symptom and the proportions of those who took medications, both before and after standardization for subgroup differences. More than 40 percent of the nearly 4000 adults surveyed reported some problems of sleeplessness and enervation, but when only those who reported persistent problems were examined, very few resorted to medications. It is concluded that the United States is not a pill popping society as depicted by the popular press. 19 references. (Author abstract modified)

**003841** Murray, Michael J.; Murray, William J. Box 3399 Station B, Vanderbilt University, Nashville, TN 37235 **Nitrous oxide availability.** Journal of Clinical Pharmacology. 20(4 Part 1):202-205, 1980.

Sources of nonprescription forms of nitrous oxide (N20) are described. N20 can be obtained in aerosol whipping cream containers from grocery stores and in charges used for dispensing whipping cream in restaurants and dairy bars. Both systems contain sufficient concentrations and volumes of N20 to deliver multiple highs. Since peripheral nerve damage, mitotic poisoning of bone marrow, psychosis, and mental impairment have been associated with N20, its nonprescription distribution should be discontinued. 26 references.

**003842** OBrien, Joanne. St. Luke's Methodist Hospital, Cedar Rapids, IA **Teaching psychiatric inpatients about their medications.** Journal of Psychiatric Nursing and Mental Health Services. 17(10):30-32, 1979.

A medication education program for psychiatric inpatients is described. The program was designed to increase compliance, to decrease abuse/misuse, to provide support in coping with medication effects, and to increase the patient's understanding of his illness and responsible participation in its treatment. An initial verbal quiz provides immediate feedback on the patients' knowledge of medications and their actions, and specially developed audiovisuals provide patients with medication information. A model, explaining catecholamine theory is presented and integrated with explanation of drug actions; and hints for dealing with drug side-effects are covered. Patients are also able to discuss problems and questions with doctors. Patient response to these classes has been very positive; and a teaching plan has been developed as part of the hospital's patient education program. 8 references.

**003843** OBrien, Richard D. no address **The receptors: a comprehensive treatise. Vol. 1, general principles and procedures.** New York, Plenum Press, 1979. 361 p.

General principles and investigatory procedures for studying receptor systems are described. Topics discussed include: the effects of various drugs on receptors, definitions of receptors; black lipid membranes; nucleotide cyclase.

**003844** Pohl, Richard W.; Revusky, Sam; Mellor, Clive S. Memorial University of Newfoundland, St. John's, Newfoundland, Canada A1B 3X9 **Drugs employed in the treatment of alcoholism: rat data suggest they are unnecessarily severe.** Behaviour Research and Therapy. 18(2):71-78, 1980.

Two experiments were conducted to challenge the view that the effectiveness of drugs used in chemical aversion therapy (CAT) and deterrent therapy of alcoholism depends on their degree of noxiousness. Five noxious drugs (emetine, ipecac, succinylcholine, calcium carbimide, and disulfiram) which are used with lithium were evaluated for their ability to reduce rats' drinking of a familiar, readily consumed ethanol solution. The lithium dosage was equivalent in terms of body weight to the largest daily recommended human dose, while that of the drugs was twice this equivalent. Despite the use of comparatively smaller doses of lithium, none of the noxious drugs produced stronger ethanol aversions than lithium. This supports the use of lithium in CAT and suggests that unnecessarily noxious drugs are being used in the treatment of alcoholism. 20 references. (Author abstract modified)

**003845** Priest, R. G.; Pletscher, A.; Ward, J. no address **Sleep research.** Lancaster, England, MTP Press, 1979. 224 p. L7.95.

The proceedings of the Northern European Symposium on Sleep are reproduced. Sleep research, particularly that involving study of aspects of benzodiazepines, is presented and followed by discussion. The first section on physiology and pathophysiology of sleep deals with some biochemical aspects indicating that benzodiazepines are bound to a specific target site in the brain. The second and third sections deal with the treatment of sleep disorders, parameters of efficiency, and clinical experience. Research on a wide range of both well established and new hypnotics includes pharmacodynamics and comments on usage.

**003846** Rees, W. Linford. St. Bartholomew's Hospital, West Smithfield, London EC1A 7BE, England **Psychotropic drugs: uses in medical and psychosomatic disorders.** Psychosomatics. 20(12):837-839, 1979.

A brief review of the clinical use of the major classes of psychotropic drugs is presented. Briefly discussed are the neuroleptics, anxiolytics, stimulants, antidepressants, beta blockers, and lithium. In the management and treatment of psychosomatic disorders, psychotropic drugs are most useful as a tactical aid in general patient care strategy. It is noted that treatment must also take into account the role played by social and psychological factors such as interpersonal difficulties, stressful life situations, and the patient's personality. It is concluded that psychotropic drugs can play an important part in the general strategy of treatment.

**003847** Rossner, Mahnolf. Neurologisch-Psychiatrische Klinik der Medizinischen Akademie DDR-8019 Dresden, Germany / **The question of surgical castration of sexual delinquents: formation./** Zur Frage der operativen Kastration von Sexualdelinquenten -- Aktuelle Literaturubersicht und der Ansatz einer Meinungsbildung. Psychiatrie, Neurologie und Medizinische Psychologie. 31(6):321-328, 1979.

A survey of topical literature on the surgical castration of sexual delinquents is presented and an attempt is made to form an opinion regarding the indications for such as operation. The research of Langeluddeke and Wiechert is discussed and an overview of various methods of treatment for cases of sexual deviation/sexual delinquency is given. These methods include: surgical/pharmacological castration, combined psychotherapy and pharmacological castration, and stereotactic surgery on the hypothalamus. 44 references. (Journal abstract modified)

**003848** Salem, Ronald S.; Muniz, Carlos E. Dept. of Psychiatry (573/116A), Veterans Administration Hospital, Gainesville, FL 32602 **Treatment of propoxyphene dependence with thioridazine.** Journal of Clinical Psychiatry. 41(5):179-181, 1980.

The successful use of thioridazine in the treatment of a propoxyphene dependent patient is presented. The patient admitted taking capsules by mouth in amounts varying from 2,000 to 3,000mg daily, usually in divided doses, three to four times a day. Treatment consisting of gradual stepwise reduction of both the propoxyphene and diazepam had been planned, but acute episodes of craving and restlessness encouraged the physicians to initiate thioridazine which provided quick relief from these episodes. Since thioridazine was successful in this case, the use of this drug is suggested in the management of the withdrawal symptoms associated with propoxyphene and other similar drugs. 15 references. (Author abstract modified)

**003849** Schwarcz, Glenn. OMalley Division, Saint Elizabeths Hospital, Washington, DC 20032 **Serum lithium spot checks for manic-depressive patients.** American Journal of Psychiatry. 137(6):744-745, 1980.

The necessity of conducting serum lithium spot checks for manic depressed patients is highlighted in two case histories. Both patients did not comply with their medication routines. Each had stopped their prescribed use of lithium and then loaded up on lithium right before they were checked by their doctors. Because of this, their manic states returned. It is argued that a spot check of lithium levels without any warning to the patients would encourage them to comply with their drug routine.

**003850** Simon, P. no address **Neurotransmitters (proceedings of the 7th International Congress of Pharmacology, vol 2.)** New York, Pergamon Press, 1979. 312 p. Vol. 2. $50.00.

Proceedings from three symposia of the 7th International Congress of Pharmacology, held in Paris in 1978, on gamma-aminobutyric acid (GABA), CNS neurotransmitter interdependence, and new perspectives on neurotransmitters, are presented. Summaries of recent work on neurotransmitters undertaken by a variety of researchers are presented. Topics discussed include: use of benzodiazepine to prove the molecular mechanisms participating in the supramolecular function of the GABA receptors; GABA studies from a psychopharmacological viewpoint; GABA studies from a classical pharmacological viewpoint; the importance of GABA in the mammalian central nervous system; histamine; substance-P; and neurotransmitter codes in the brain.

**003851** Strian, F.; Albert, W.; Klicpera, C. Max-Planck-Inst. f. Psychiatrie, Klinisches Inst., Kraepelinstrasse 10, D-8000 Munich 40, Germany **Course of depressive mood and psychomotor activation in endogenous depression.** Archiv fur Psychiatrie und Nervenkrankheiten. 227(3):193-206, 1979.

The course of the depressive mood during depressive phases was measured by a self-rating mood scale and analyzed by various algorithms. Agitated, depressed patients revealed a continuous decline in the depressive mood; retarded, depressed patients, on the other hand, showed brief and marked mood fluctuations during remission. Although various effects occured due to treatment, especially differences between the effects of electroconvulsive therapy and antidepressants, these changes in mood are seen as predominantly due to psychomotor activation. The relationship between these courses of depression is discussed and interpreted on the basis of biochemical and psychopharmacological findings. 35 references. (Author abstract)

**003852** Tognoni, G.; Bellantuono, C.; Bonati, M.; DIncalci, M.; Gerna, M.; Latini, R.; Mandelli, M.; Porro, M. G.; Riva, E. Laboratory of Clinical Pharmacology, Istituto di Ricerche Farmacologiche **Clinical relevance of pharmacokinetics.** Clinical Pharmacokinetics. 5(2):105-136, 1980.

Recent publications in the field of pharmacokinetics are reviewed in order to assess their relevance to therapeutic practice. After careful analysis of publications on some of the most representative drugs and drug groups, tentative guidelines are given for data for which the clinical relevance is well established, for findings for which the relevance should be checked in routine practice, for areas where much research is still needed before kinetic knowledge can result in improved therapeutic outcome, and for fields where only minor therapeutic advances can be expected from extended kinetic investigation. Within the general framework of clinical pharmacology, it appears that the use of pharmacokinetics is a fundamental research tool and a useful aid to therapeutic practice only if its limitations are clearly recognized and if priority is given to creating favorable, controlled conditions for good diagnostic practice, for general patient care, and for compliance of the patient with treatment. A restricted attitude is suggested toward the natural expansion of blood level monitoring, because of the risk that doctors and institutions become dependent on this technique and lose their critical capacity in the use of both clinical and kinetic data. 254 references. (Author abstract modified)

**003853** van Praag, H. M. Dept. of Psychiatry, State University of Utrecht, Utrecht, The Netherlands **/Psychotherapy vs. pharmacotherapy in the treatment of psychiatric patients./** Tablets and talking -- a spurious contrast in psychiatry. Comprehensive Psychiatry. 20(6):502-510, 1979.

The view that psychotherapy, not the administration of psychotropic drugs, is the preferred therapy in psychiatric cases of psychogenic or psychosocial overtones is disputed. It is argued that psychosocially determined behavior disorders also have a neurochemical substrate and it is sensible to attempt to normalize behavior by correction of this substrate. In addition, normalization of the cerebral substrate with the aid of pharmacother-

apy is no less a causal type of therapy than is reduction of the pathogenic input with the aid of psychotherapy. Pharmacotherapy and psychotherapy are complementary; each separately is an incomplete therapy. This argument is considered as valid where psychotropic drugs with a relatively specific effect are available, as they are for the vital depressions and psychoses of the schizophrenic type. 30 references.

**003854** Weal, Elizabeth; Sigel, George. Sigel: West Broadway Unit, Bay Cove (Tufts) Mental Health Center, 62 Joyce-Hayes Way, South Boston, MA 02127 Innovations. 6(3):32-33, 1979.

A no medication medication clinic, stemming from staff concern about the risks of long-term antipsychotic medication, is reported. Of 50 patients attending the clinic, five received no medication, and 30 have been able to stop or greatly reduce their dosages of major tranquilizers while relying on the clinic and a minor tranquilizer taken on an as needed basis. Medication clinic patients attend the clinic for 45 min to 1 hr once a week or once every 2 weeks. During clinic visits, patients interact informally with other patients and meet privately with a staff member for 5 or 10 min. Many patients appear to require no maintenance medication once they have established successful relationships with clinic staffs. Experience at the clinic suggests that many patients in community based aftercare are receiving medication they may not need. 2 references.

**003855** Williams, Robert L. Dept. of Psychiatry, Baylor College of Medicine, Houston, TX **Sleeping-pill insomnia.** Journal of Clinical Psychiatry. 41(5):153-154, 1980.

Areas covered in the Institute of Medicine's (IOM) study, findings and recommendations of this comprehensive report are summarized. The chapters include an overview of sleep and medication; epidemiology of sleep complaints and prescribing practices; public health problems associated with the use of hypnotic drugs; insomnia, research findings, diagnostic approaches, and therapeutic options; sleep disturbance in the elderly; and conclusions. The IOM study reveals a decline in hypnotic prescriptions in the past 7 years, and that physicians have switched from prescribing barbituates to prescribing flurazepam. Recommendations include: 1) close monitoring by the physician of all patients receiving hypnotic drugs, and limiting the number prescribed to cover a few nights only, 2) particular care in the choice of medications for selected groups such as elderly patients, and 3) availability of clearest possible directions and warnings for patients about the use of hypnotic drugs. 5 references.

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